Access DB# 80301

# SEARCH REQUEST FORM

**Scientific and Technical Information Center**

11/15/02

Requester's Full Name: David Lukton Examiner # : 71263 Date:

Art Unit: 1653 Phone Number 308-3213 Serial Number: 09-728653

Mail Box and Bldg/Room Location: Results Format Preferred (circle): PAPER DISK E-MAIL

Mailbox: 9B01 ; Exr Rm: 9B05

**If more than one search is submitted, please prioritize searches in order of need.**

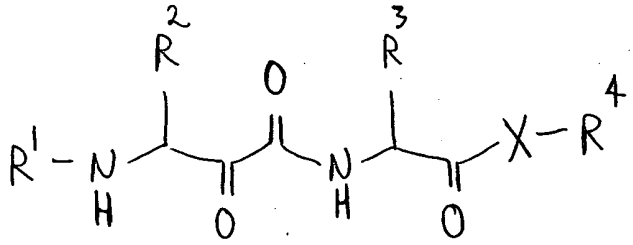
**********

Title: *alpha*-KETOAMIDE INHIBITORS OF HEPATITIS C VIRUS NS3 PROTEASE

Applicant: Wei Han

Earliest Priority Date: 12/3/99

* * * *



R1 = anything

R2 = anything

R3 = anything

R4 = anything

X = -NH- or -O-



**********

| **STAFF USE ONLY** | **Type of Search** | **Vendors and cost where applicable** |
|---|---|---|
| Searcher: | NA Sequence (#) | STN |
| Searcher Phone #: Point of Contact P. Sheppard | AA Sequence (#) | Dialog |
| Searcher Location: Telephone number: (703) 308-4499 | Structure (#) | Questel/Orbit |
| Date Searcher Picked Up: | Bibliographic | Dr.Link |
| Date Completed: 11/18/02 | Litigation | Lexis/Nexis |
| Searcher Prep & Review Time: | Fulltext | Sequence Systems |
| Clerical Prep Time: | Patent Family | WWW/Internet |
| Online Time: | Other | Other (specify) |

PTO-1590 (8-01)

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=> fil hcaplus
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FILE COVERS 1907 - 18 Nov 2002  VOL 137 ISS 21
FILE LAST UPDATED: 17 Nov 2002  (20021117/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

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L1                STR
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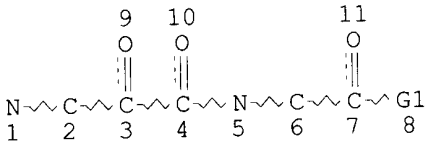


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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  11

STEREO ATTRIBUTES: NONE
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L4                STR
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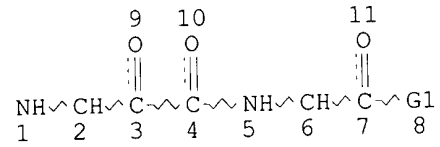


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VAR G1=NH/O
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE

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| L5 | 1955 SEA | FILE=REGISTRY SUB=L3 SSS FUL L4 | |
| L6 | 68 SEA | FILE=HCAPLUS ABB=ON PLU=ON | L5 |
| L7 | 44 SEA | FILE=HCAPLUS ABB=ON PLU=ON | L6 AND PD<DECEMBER 3 1999 |
| L8 | 17584 SEA | FILE=REGISTRY ABB=ON PLU=ON | PROTEASE? OR PROTEINASE? |
| L9 | 173122 SEA | FILE=HCAPLUS ABB=ON PLU=ON | L8 OR PROTEASE? OR PROTEINASE? |
| L10 | 24 SEA | FILE=HCAPLUS ABB=ON PLU=ON | L9 AND L7 |
| L11 | 7 SEA | FILE=HCAPLUS ABB=ON PLU=ON | L10 AND ?KETOAMI? |

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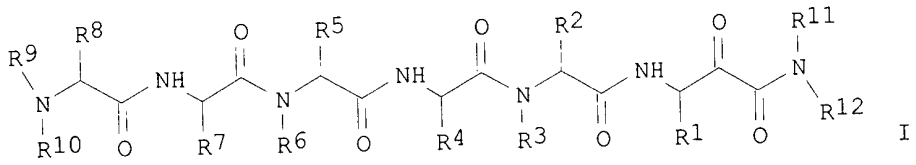
=>

=> d ibib abs hitrn l11 1-7

L11 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:760024 HCAPLUS
DOCUMENT NUMBER: 132:93653
TITLE: Preparation of .alpha.-**ketoamide** peptides as antiviral HCV **proteinase** inhibitors
INVENTOR(S): Hurst, David Nigel; Jones, Philip Stephen; Kay, Paul Brittain; Raynham, Tony Michael; Wilson, Francis Xavier
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: Fr. Demande, 130 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| FR 2778406 | A1 | 19991112 | FR 1999-5650 | 19990504 | <-- |
| US 6187905 | B1 | 20010213 | US 1999-305030 | 19990504 | |
| IT 1312558 | B1 | 20020422 | IT 1999-MI950 | 19990504 | |
| GB 2338482 | A1 | 19991222 | GB 1999-10384 | 19990505 | |
| ES 2165269 | A1 | 20020301 | ES 1999-918 | 19990505 | |
| JP 11349597 | A2 | 19991221 | JP 1999-125419 | 19990506 | |
| DE 19920966 | A1 | 20000113 | DE 1999-19920966 | 19990506 | |

PRIORITY APPLN. INFO.: GB 1998-9664 A 19980506
OTHER SOURCE(S): MARPAT 132:93653
GI




I

AB .alpha.-**Ketoamide** peptides I (R1 = alkyl, haloalkyl, cyanoalkyl, aralkyl, thioalkyl, heteroalkyl, alkenyl, alkynyl; R2 = alkyl, hydroxyalkyl, carboxyalkyl, aralkyl, aminocarbonylalkyl, cycloalkyl, arylalkoxyalkyl; R3, R6, R9 = independently H, alkyl; R2R3 = alkylidene;

R4 = alkyl, hydroxyalkyl, cycloalkyl, carboxyalkyl, arylalkyl, arylalkoxyalkyl, thioalkyl, cyanoalkyl, alkenyl, aryl, heteroarylalkyl, arylsulfonylalkyl, acetamidothioalkyl, cycloalkyl; R5 = alkyl, hydroxyalkyl, thioalkyl, aralkyl, cyanoalkyl, thioalkyl, cycloalkyl, arylalkoxyalkyl, aryl, arysulfonylguanidinoalkyl, heteroarylalkyl; R7 = H, alkyl, carboxyalkyl, hydroxyalkyl, arylalkyl, cycloalkyl, heteroarylalkyl, nitroguanidinoalkyl, thioalkyl, arylalkoxycarbonylalkyl, formamidoalkyl; R8 = alkyl, cycloalkyl, carboxyalkyl, arylalkoxyalkyl, mercaptoalkyl, aryl, nitroguanidinoalkyl, thioalkyl, formamidoalkyl; R8R9 = sulfur-contg, trimethylene; R10 = alkyl, alkoxyalkylcarbonyl, acyl; R11, R12 = independently H, alkyl, aryl, arylalkyl, cycloalkyl, alkoxy, OH) were prepd. as HCV **proteinase** inhibitors and antiviral agents. 3(RS)-[[N-[N-[N-[N-[N-(3-carboxypropionyl)-L-.alpha.-aspartyl]-L-.alpha.-glutamyl]-2-methyl-L-phenylalanyl]-3-methyl-L-valyl]-L-leucyl]amino]-5,5,5-trifluoro-N-[1(S)-2-naphthylethyl]-2-oxovaleramide was prepd. as antiviral HCV **proteinase** inhibitor (EC50 = 0.004 .mu.mol/L).

IT **254437-29-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of .alpha.-**ketoamide** peptides as antiviral HCV **proteinase** inhibitors)

IT **9001-92-7, Proteinase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prepn. of .alpha.-**ketoamide** peptides as antiviral HCV **proteinase** inhibitors)

IT **254437-27-9P 254437-28-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of .alpha.-**ketoamide** peptides as antiviral HCV **proteinase** inhibitors)

L11 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:249080 HCAPLUS
DOCUMENT NUMBER: 130:281997
TITLE: Quinoline-containing .alpha.-**ketoamide** cysteine and serine **protease** inhibitors
INVENTOR(S): Chatterjee, Sankar; Mallamo, John P.; Dunn, Derek Douglas; Josef, Kurt Allen; Gu, Zi-qiang; Daines, Robert A.; Kingsbury, William Dennis; Pendrak, Israel; Sham, Kelvin C.
PATENT ASSIGNEE(S): Cephalon Inc., USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9917775 | A1 | 19990415 | WO 1998-US21054 | 19981007 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6083944 | A | 20000704 | US 1998-167193 | 19981006 |
| CA 2304204 | AA | 19990415 | CA 1998-2304204 | 19981007 <-- |

| | | | | |
|---|---|---|---|---|
| AU 9897882 | A1 | 19990427 | AU 1998-97882 | 19981007 <-- |
| AU 749099 | B2 | 20020620 | | |
| EP 1032393 | A1 | 20000906 | EP 1998-952109 | 19981007 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| JP 2001518506 | T2 | 20011016 | JP 2000-514646 | 19981007 |
| PRIORITY APPLN. INFO.: | | | US 1997-61267P P | 19971007 |
| | | | US 1998-167193 A | 19981006 |
| | | | WO 1998-US21054 W | 19981007 |

OTHER SOURCE(S): MARPAT 130:281997

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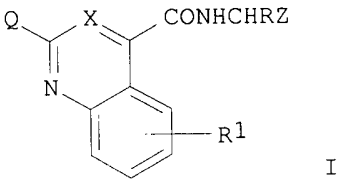



I

AB Quinoline-contg. .alpha.-keto amides I [X = CH, N, CQ1 (at least one of Q or Q1 = H); R = H, alkyl, arylalkyl, etc.; R1 = H, halo, cyano, NO2, etc.; Q, Q1 = H, alkyl, cycloalkyl, OH, alkoxy, etc.; Z = COCONHR7 and R7 = alkyl, alkenyl, alkynyl, etc.], inhibitors of cysteine and serine **proteases**, were prepd. E.g., I (Q = PhC.tplbond.C; X = CH; R = CH2Ph; Z = COCONHCH2CF3) was prepd. Inhibition of cathepsin B, .alpha.-chymotrypsin, and calpain I by I was investigated.

IT **78990-62-2**, Calpain
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(I; prepn. of quinoline-contg. .alpha.-**ketoamide** cysteine and serine **protease** inhibitors)

IT **222959-78-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of quinoline-contg. .alpha.-**ketoamide** cysteine and serine **protease** inhibitors)

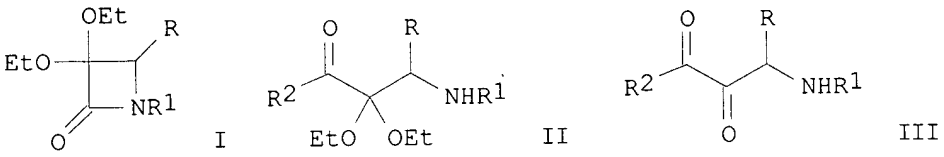
IT **37259-58-8**, Serine **protease** **37353-41-6**, Cysteine **protease**
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(prepn. of quinoline-contg. .alpha.-**ketoamide** cysteine and serine **protease** inhibitors)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2002 ACS

| | |
|---|---|
| ACCESSION NUMBER: | 1999:180641 HCAPLUS |
| DOCUMENT NUMBER: | 130:267755 |
| TITLE: | Solid and solution phase synthesis of .alpha.-keto amides via azetidinone ring-opening: application to the synthesis of poststatin |
| AUTHOR(S): | Khim, Seock-Kyu; Nuss, John M. |
| CORPORATE SOURCE: | Chiron Corporation, Emeryville, CA, 94608-2916, USA |
| SOURCE: | Tetrahedron Letters (**1999**), 40(10), 1827-1830<br>CODEN: TELEAY; ISSN: 0040-4039 |
| PUBLISHER: | Elsevier Science Ltd. |
| DOCUMENT TYPE: | Journal |
| LANGUAGE: | English |

OTHER SOURCE(S): CASREACT 130:267755
GI



I II III

AB 3,3-Diethoxy-N-sulfonyl- and -carbamoylazetidin-2-ones I [R = Ph, Et; R1 = tosyl (Ts), allyloxycarbonyl (Alloc)] undergo efficient ring-opening reaction with various amine nucleophiles to give protected **ketoamides** II (R2 = NHCH2C6H4OMe-4, furfurylamino, morpholino, Val-OMe, L-phenylalaninol, Wang resin-bound phenylalanine). Subsequent acid hydrolysis of the ketal moiety generated .alpha.-keto amides III in excellent overall yields. The naturally occurring serine **protease** inhibitor poststatin, H-Val-Val-NHCHEtCOCO-D-Leu-Val-OH, was synthesized using this ring-opening reaction as the key step.

IT **160866-54-6P 222406-19-1P 222406-31-7P**
**222406-34-0P 222406-35-1P 222406-36-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid and soln. phase synthesis of keto amides via ring opening of protected diethoxyazetidinones with amines)

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:476813 HCAPLUS
DOCUMENT NUMBER: 125:143327
TITLE: Preparation of .alpha.-**ketoamide** derivatives as cathepsin L inhibitors.
INVENTOR(S): Sohda, Takashi; Fujisawa, Yukio; Yasuma, Tsuneo; Mizoguchi, Junji
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9616079 | A2 | 19960530 | WO 1995-JP2389 | 19951124 <-- |
| WO 9616079 | A3 | 19960912 | | |
| W: AL, AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, US, UZ, VN | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| JP 08208462 | A2 | 19960813 | JP 1995-304852 | 19951122 <-- |
| AU 9539358 | A1 | 19960617 | AU 1995-39358 | 19951124 <-- |
| EP 793673 | A1 | 19970910 | EP 1995-937173 | 19951124 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |

PRIORITY APPLN. INFO.: JP 1994-290132 19941124
WO 1995-JP2389 19951124

OTHER SOURCE(S): MARPAT 125:143327
AB R4QNHCHR1COCONR5R6 [Q = bond, 1 or 2 (substituted) amino acid residues R1,

R5, R6 = H, (substituted) hydrocarbyl, heterocyclyl; R4 = acyl, (esterified) carboxyl; R5R6 = atoms to form a ring], were prepd. Thus, N-benzyloxycarbonylisoleucyl-(2R,3S)-3-amino-2-hydroxy-4-phenylbutyric acid benzylamide was stirred with 1-ethyl-3-(3-dimethylaminopropyl)carbidiimide hydrochloride and pyridinium trifluoroacetate in Me2SO/PhMe to give 83% N-benzyloxycarbonylisoleucyl-(2R,3S)-3-amino-2-oxo-4-phenylbutyric acid. The latter inhibited cathepsin L with IC50 = 1.1 .times. 10-8 M.

IT **60616-82-2**, Cathepsin L
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(inhibitors; prepn. of .alpha.-**ketoamide** derivs. as cathepsin L inhibitors)

IT **179549-80-5P 179549-81-6P 179549-83-8P 179549-84-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of .alpha.-**ketoamide** derivs. as cathepsin L inhibitors)

L11 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:731521 HCAPLUS
DOCUMENT NUMBER: 123:144653
TITLE: Preparation of peptide .alpha.-**ketoamides** as calpain inhibitors.
INVENTOR(S): Harbeson, Scott L.; Straub, Julie Ann
PATENT ASSIGNEE(S): Alkermes, Inc., USA
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9500535 | A1 | 19950105 | WO 1994-US6497 | 19940609 <-- |
| W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, UZ, VN | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 5541290 | A | 19960730 | US 1993-82274 | 19930624 <-- |
| AU 9472452 | A1 | 19950117 | AU 1994-72452 | 19940609 <-- |

PRIORITY APPLN. INFO.: US 1993-82274 19930624
WO 1994-US6497 19940609

OTHER SOURCE(S): MARPAT 123:144653

AB M(A1)xA2NHCHR1COCONHR2SO2R3 (sic), M(A1)xA2NHCHR1COCONHR5R6, etc.; [M = H, H2NCO, H2NCS, H2NSO2, R7CS, R7NHCS, R7CO, R7SO2, R7O2C, etc.; R7 = 1-adamantyl, (substituted) alkyl, alkyl, Ph, naphthyl, phenylalkyl, phenoxyalkyl, etc.; A1 = D-, L-, or nonchiral amino acid, e.g., Ala, Val, Leu, Ile, Met, Tyr, Asn, Gln, .beta.-Ala, Sar, Orn, O-ethylserine, pipecolinic acid, cyclohexylalanine, pyridylalanine, p-nitrophenylalanine, .alpha.-aminoheptanoic acid, citrulline, 2-azetidinecarboxylic acid, trifluoroleucine, etc.; x = 0-3; A2 = D- or L-amino acid capable of imparting calpain specificity; R1 = alkyl, cycloalkyl, fluoroalkyl; R2 = alkyl, cycloalkyl, phenylalkyl, (substituted) phenylalkyl, phenylcycloalkyl; R3 = R2, OH, OR2, NH2, NHR2; NR2R2; R5, R6 = H, alkyl, cycloalkyl, (substituted) phenylalkyl, phenylcycloalkyl, morpholinoalkyl, piperidinoalkyl, etc.], were prepd. Thus, Z-Leu-Abu-CONHEt (Abu = L-.alpha.-aminobutyric acid) (soln. phase prepn. given) inhibited calpain I with Ki = 77 nM.

IT **160801-90-1P 160801-92-3P 166195-97-7P**
**166195-98-8P 166195-99-9P 166196-00-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptide .alpha.-**ketoamides** as calpain inhibitors)
IT **78990-62-2**, Calpain
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(prepn. of peptide .alpha.-**ketoamides** as calpain inhibitors)

L11 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:266967 HCAPLUS
DOCUMENT NUMBER: 122:56583
TITLE: Preparation of arginine keto-amide derivative antithrombotics.
INVENTOR(S): Webb, Thomas Roy; Miller, Todd Anthony; Vlasuk, George Phillip; Abelman, Matthew Mark
PATENT ASSIGNEE(S): Corvas International, Inc., USA
SOURCE: PCT Int. Appl., 188 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| WO 9408941 | A1 | 19940428 | WO 1993-US10015 | 19931018 | <-- |
| W: AU, CA, JP | | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | | |
| US 5371072 | A | 19941206 | US 1992-962301 | 19921016 | <-- |
| AU 9454081 | A1 | 19940509 | AU 1994-54081 | 19931018 | <-- |
| AU 678189 | B2 | 19970522 | | | |
| EP 664786 | A1 | 19950802 | EP 1993-924369 | 19931018 | <-- |
| EP 664786 | B1 | 19990324 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | | |
| JP 08502493 | T2 | 19960319 | JP 1993-510359 | 19931018 | <-- |
| AT 178044 | E | 19990415 | AT 1993-924369 | 19931018 | <-- |

PRIORITY APPLN. INFO.: US 1992-962301 19921016
WO 1993-US10015 19931018

OTHER SOURCE(S): MARPAT 122:56583
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. [I; A1 = R1CO, R1O2C, R1NHCO, R1SO2, R1OSO2, R1NHSO2; R1 = alkyl, alkenyl, (substituted) aryl, aralkyl, aralkenyl, perfluoroalkyl, perfluoroaryl, trimethylsilylalkyl, etc.; A2 = H, alkyl, alkenyl, aryl, aralkyl, aralkenyl, tetrazolylalkyl, (CH2)mCO2H, (CH2)mSO3H, etc.; A3 = Ala, Gly, Ile, Leu, Orn, Pro, L-azetidinecarboxylate, L-methionine sulfone, L-pipecolic acid residues, etc.; A4 = Q1, Q2, NHR5, etc.; p, q = 1-5; p + q = 4-8; r = 0-3; R4 = (substituted) aryl; R5 = aryl; R6 = H, alkyl; R7 = H, (substituted) alkyl, aryl, aralkyl], were prepd. Thus, title compd. II, prepd. by soln. phase methods, at 0.5 mg/kg i.v. bolus + 100 mg/kg/min i.v. in an extracorporeal shunt model in rats reduced clot size from 41.30 mg (controls) to 10.20 mg.
IT **159945-32-1P 159945-35-4P 159945-38-7P**
**159945-41-2P 159945-42-3P 159945-43-4P**
**159945-50-3P 159945-53-6P 159945-54-7P**

**159945-55-8P 159946-39-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as antithrombotic)

IT **159945-82-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for **ketoamide** antithrombotic)

L11 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:485791 HCAPLUS
DOCUMENT NUMBER: 117:85791
TITLE: Novel tight-binding inhibitors of leukotriene A4 hydrolase
AUTHOR(S): Yuan, Wei; Wong, Chi Huey; Haeggstroem, Jesper Z.; Wetterholm, Anders; Samuelsson, Bengt
CORPORATE SOURCE: Dep. Chem., Scripps Res. Inst., La Jolla, CA, 92037, USA
SOURCE: Journal of the American Chemical Society (**1992**), 114(16), 6552-3
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several .alpha.-keto-.beta.-amino esters were developed as tight-binding, transition-state analog inhibitors of leukotriene A4 hydrolase, a Zn2+-enzyme which possesses both epoxide hydrolase and amidase activities. The inhibitor design combines advantages based on the tight binding of leukotriene substrate and a better understanding of the transition-state nature of Zn2+-**protease** reactions.
IT **142699-25-0**
RL: BIOL (Biological study)
(leukotriene A4 hydrolase inhibition by, structure in relation to)

=>
=>

=> select hit rn l11 1-7
E1 THROUGH E38 ASSIGNED

=> fil reg
FILE 'REGISTRY' ENTERED AT 09:45:14 ON 18 NOV 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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STRUCTURE FILE UPDATES: 15 NOV 2002 HIGHEST RN 473758-49-5
DICTIONARY FILE UPDATES: 15 NOV 2002 HIGHEST RN 473758-49-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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=> d his l12

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               SELECT HIT RN L11 1-7

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L12           38 S E1-E38

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=>

=> d ide can l12 1-38

L12  ANSWER 1 OF 38  REGISTRY  COPYRIGHT 2002 ACS
RN   254437-29-1  REGISTRY
CN   Glycinamide, N-(3-carboxy-1-oxopropyl)-L-.alpha.-aspartyl-L-.alpha.-
     glutamyl-2-methyl-L-phenylalanyl-3-methyl-L-valyl-L-leucyl-3-amino-5,5,5-
     trifluoro-2-oxopentanoyl-N-methyl- (9CI)  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C43 H61 F3 N8 O15
SR   CA
LC   STN Files:   CA, CAPLUS, USPATFULL

Absolute stereochemistry.
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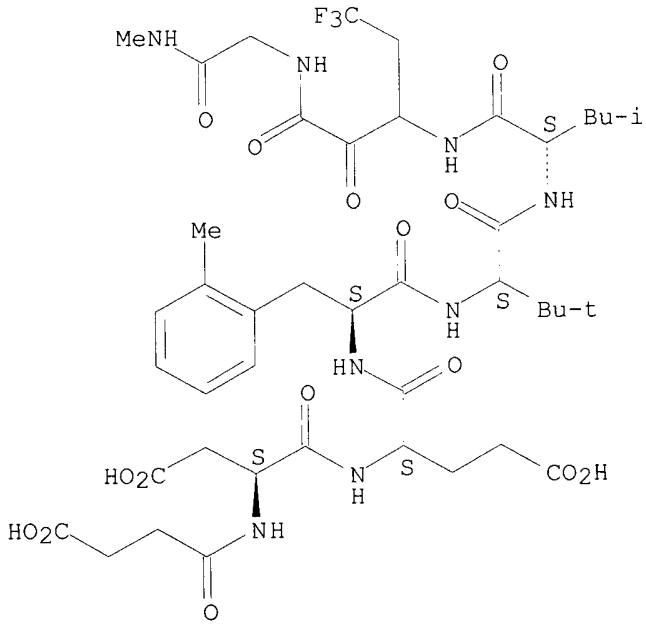


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                1 REFERENCES IN FILE CA (1962 TO DATE)
                1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE   1:  132:93653
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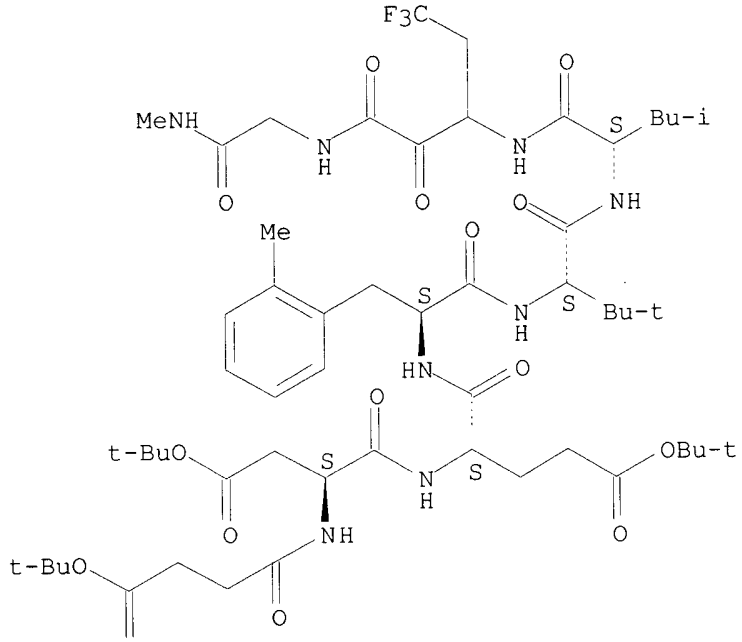
L12 ANSWER 2 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **254437-28-0** REGISTRY
CN Glycinamide, N-[4-(1,1-dimethylethoxy)-1,4-dioxobutyl]-L-.alpha.-aspartyl-L-.alpha.-glutamyl-2-methyl-L-phenylalanyl-3-methyl-L-valyl-L-leucyl-3-amino-5,5,5-trifluoro-2-oxopentanoyl-N-methyl-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C55 H85 F3 N8 O15
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

PAGE 1-A

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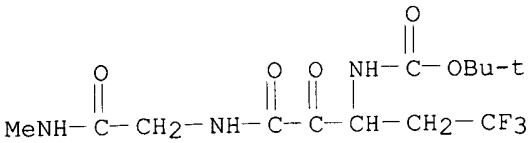
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 132:93653

L12 ANSWER 3 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **254437-27-9** REGISTRY
CN Carbamic acid, [3-[[2-(methylamino)-2-oxoethyl]amino]-2,3-dioxo-1-(2,2,2-trifluoroethyl)propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C13 H20 F3 N3 O5
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

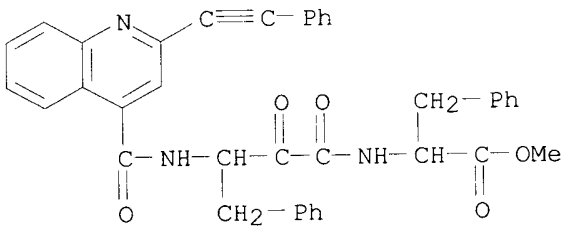


**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 132:93653

L12 ANSWER 4 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **222959-78-6** REGISTRY
CN Phenylalanine, N-[1,2-dioxo-4-phenyl-3-[[[2-(phenylethynyl)-4-quinolinyl]carbonyl]amino]butyl]-, methyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C38 H31 N3 O5
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

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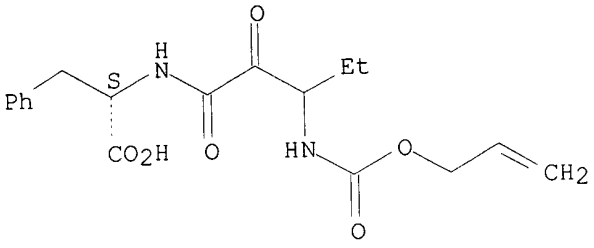
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 130:281997

L12 ANSWER 5 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **222406-36-2** REGISTRY
CN L-Phenylalanine, N-[1,2-dioxo-3-[[(2-propenyloxy)carbonyl]amino]pentyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C18 H22 N2 O6
SR CA
LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry.



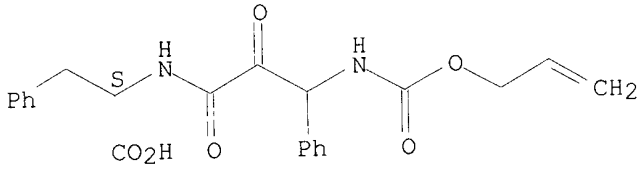
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 130:267755

L12 ANSWER 6 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **222406-35-1** REGISTRY
CN L-Phenylalanine, 2-oxo-3-phenyl-N-[(2-propenyloxy)carbonyl]-.beta.-alanyl- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C22 H22 N2 O6
SR CA
LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry.



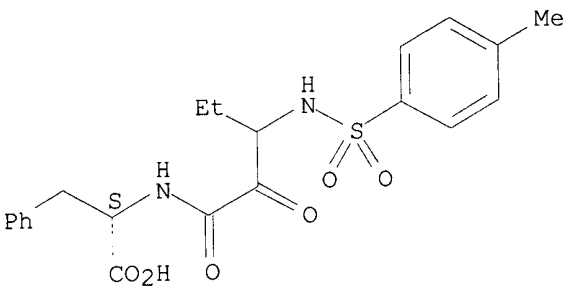
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 130:267755

L12 ANSWER 7 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **222406-34-0** REGISTRY
CN L-Phenylalanine, N-[3-[[(4-methylphenyl)sulfonyl]amino]-1,2-dioxopentyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C21 H24 N2 O6 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



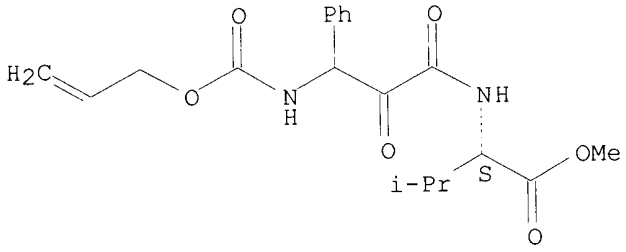
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 130:267755

L12 ANSWER 8 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **222406-31-7** REGISTRY
CN L-Valine, 2-oxo-3-phenyl-N-[(2-propenyloxy)carbonyl]-.beta.-alanyl-, methyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C19 H24 N2 O6
SR CA
LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry.



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

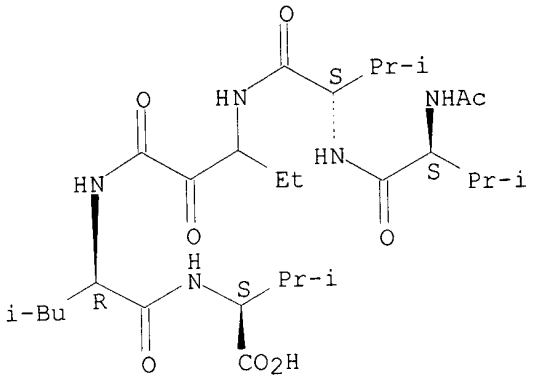
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 130:267755

L12 ANSWER 9 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **222406-19-1** REGISTRY
CN L-Valine, N-acetyl-L-valyl-L-valyl-3-amino-2-oxopentanoyl-D-leucyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C28 H49 N5 O8
SR CA
LC STN Files: CA, CAPLUS

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

Absolute stereochemistry.

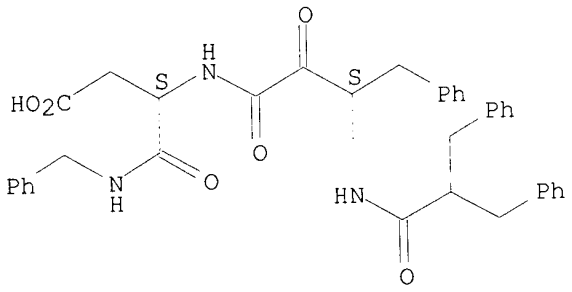


1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 130:267755

L12 ANSWER 10 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **179549-84-9** REGISTRY
CN Butanoic acid, 3-[[1,2-dioxo-3-[[1-oxo-3-phenyl-2-(phenylmethyl)propyl]amino]-4-phenylbutyl]amino]-4-oxo-4-[(phenylmethyl)amino]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C37 H37 N3 O6
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

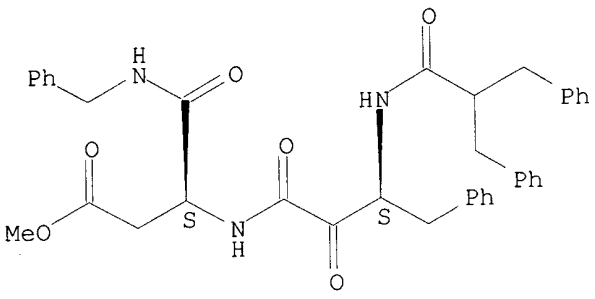
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 125:143327

L12 ANSWER 11 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **179549-83-8** REGISTRY
CN Butanoic acid, 3-[[1,2-dioxo-3-[[1-oxo-3-phenyl-2-(phenylmethyl)propyl]amino]-4-phenylbutyl]amino]-4-oxo-4-[(phenylmethyl)amino]-, methyl ester, [S-(R*,R*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C38 H39 N3 O6
SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.



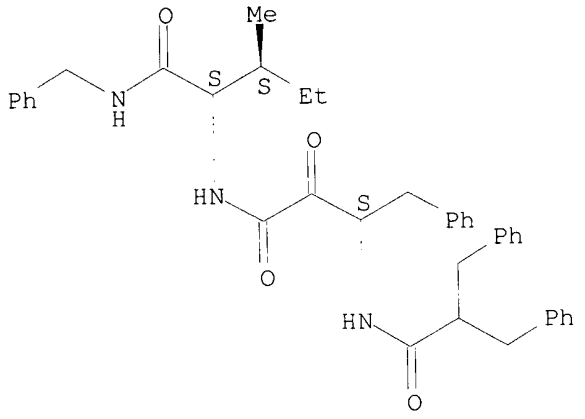
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 125:143327

L12 ANSWER 12 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **179549-81-6** REGISTRY
CN Benzenebutanamide, N-[2-methyl-1-[[(phenylmethyl)amino]carbonyl]butyl]-.alpha.-oxo-.beta.-[[1-oxo-3-phenyl-2-(phenylmethyl)propyl]amino]-, [1S-[1R*(R*),2R*]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C39 H43 N3 O4
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

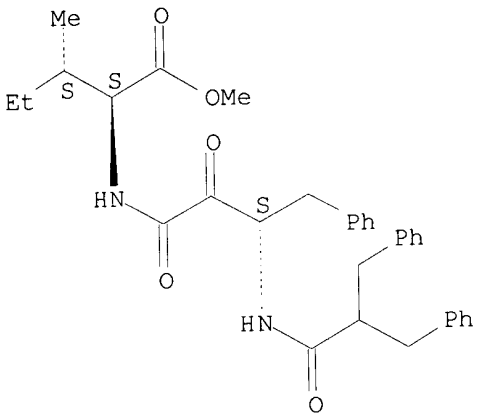
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 125:143327

L12 ANSWER 13 OF 38 REGISTRY COPYRIGHT 2002 ACS

RN **179549-80-5** REGISTRY
CN L-Isoleucine, N-[1,2-dioxo-3-[[1-oxo-3-phenyl-2-(phenylmethyl)propyl]amino]-4-phenylbutyl]-, methyl ester, [S-(R*,R*)]-(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C33 H38 N2 O5
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

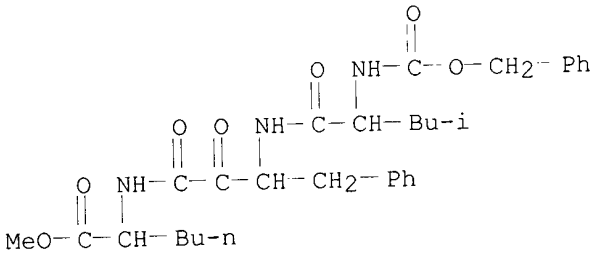


**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 125:143327

L12 ANSWER 14 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **166196-00-5** REGISTRY
CN L-Norleucine, N-[(phenylmethoxy)carbonyl]-L-leucyl-2-oxo-4-phenyl-(S)-3-aminobutanoyl-, methyl ester (9CI) (CA INDEX NAME)
MF C31 H41 N3 O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



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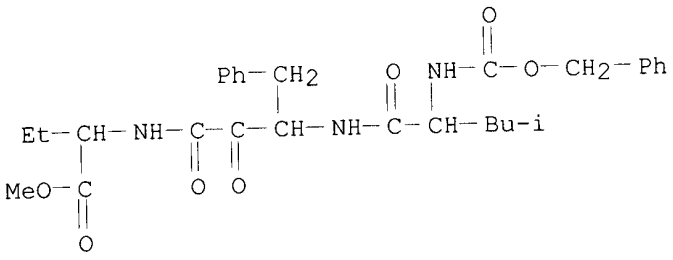
REFERENCE 1: 123:144653

L12 ANSWER 15 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **166195-99-9** REGISTRY
CN Butanoic acid, N-[(phenylmethoxy)carbonyl]-L-leucyl-2-oxo-4-phenyl(S)-3-aminobutanoyl-L-2-amino-, methyl ester (9CI) (CA INDEX NAME)
MF C29 H37 N3 O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



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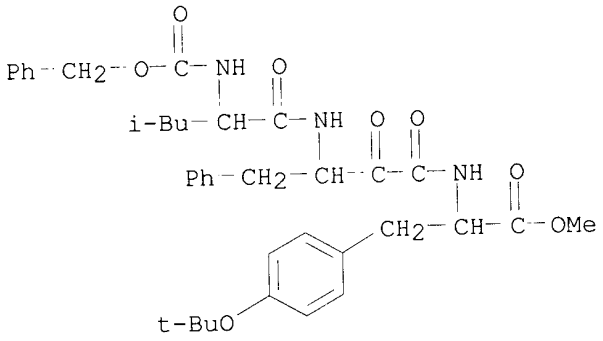
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 123:144653

L12 ANSWER 16 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **166195-98-8** REGISTRY
CN L-Tyrosine, N-[(phenylmethoxy)carbonyl]-L-leucyl-2-oxo-4-phenyl-(S)-3-aminobutanoyl-O-(1,1-dimethylethyl)-, methyl ester (9CI) (CA INDEX NAME)
MF C38 H47 N3 O8
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



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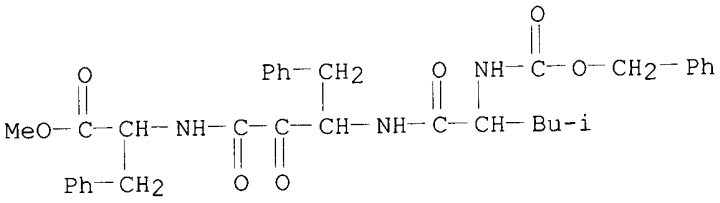
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 123:144653

L12 ANSWER 17 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **166195-97-7** REGISTRY
CN L-Phenylalanine, N-[(phenylmethoxy)carbonyl]-L-leucyl-2-oxo-4-phenyl-(S)-3-

aminobutanoyl-, methyl ester (9CI) (CA INDEX NAME)
MF C34 H39 N3 O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

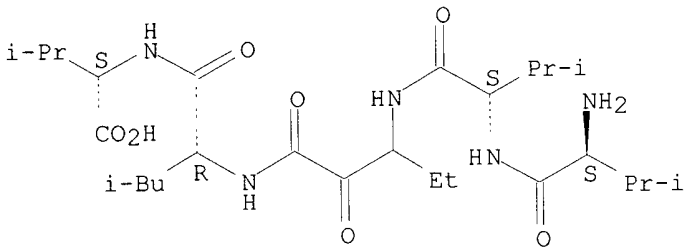
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 123:144653

L12 ANSWER 18 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **160866-54-6** REGISTRY
CN L-Valine, L-valyl-L-valyl-2-oxo-3-aminopentanoyl-D-leucyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C26 H47 N5 O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

Absolute stereochemistry.



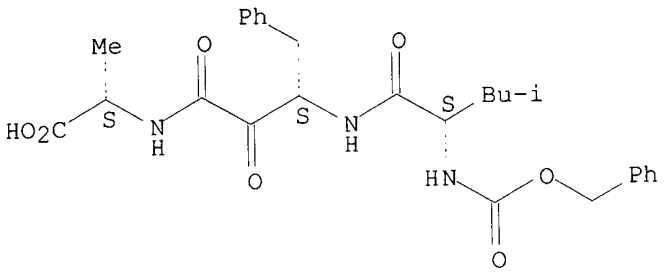
2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 130:267755

REFERENCE 2: 122:131140

L12 ANSWER 19 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **160801-92-3** REGISTRY
CN L-Alanine, N-[3-[[4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1,2-dioxo-4-phenylbutyl]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H33 N3 O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

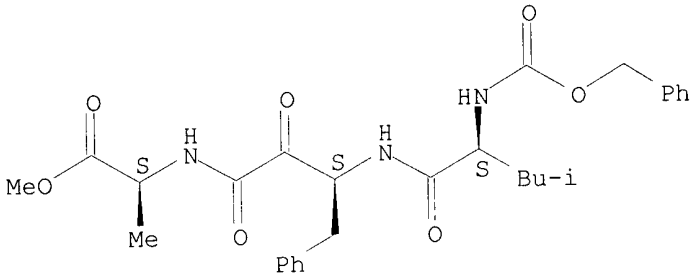
2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 123:144653

REFERENCE 2: 122:133766

L12 ANSWER 20 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **160801-90-1** REGISTRY
CN L-Alanine, N-[3-[[4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1,2-dioxo-4-phenylbutyl]-, methyl ester, [S-(R*,R*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H35 N3 O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

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2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 123:144653

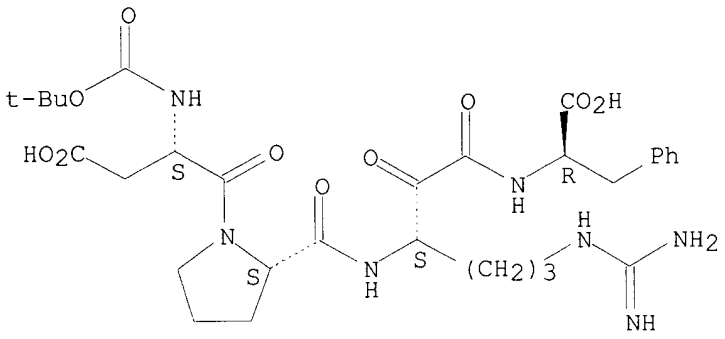
REFERENCE 2: 122:133766

L12 ANSWER 21 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **159946-39-1** REGISTRY
CN D-Phenylalanine, N-[(1,1-dimethylethoxy)carbonyl]-L-.alpha.-aspartyl-L-prolyl-(3S)-3-amino-6-[(aminoiminomethyl)amino]-2-oxohexanoyl- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:
CN D-Phenylalanine, N-[(1,1-dimethylethoxy)carbonyl]-L-.alpha.-aspartyl-L-prolyl-N6-(aminoiminomethyl)-2-oxo-(S)-3,6-diaminohexanoyl-
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C30 H43 N7 O10
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

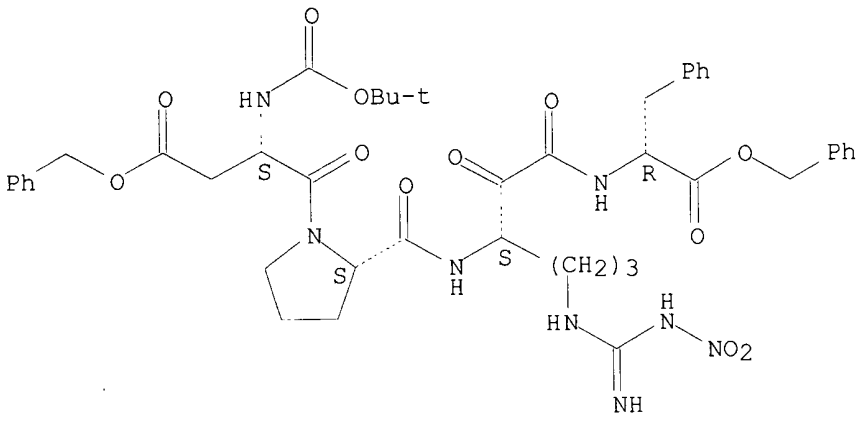
REFERENCE 1: 126:199831

REFERENCE 2: 122:56583

L12 ANSWER 22 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **159945-82-1** REGISTRY
CN D-Phenylalanine, N-[(1,1-dimethylethoxy)carbonyl]-L-.alpha.-aspartyl-L-prolyl-(3S)-3-amino-6-[[imino(nitroamino)methyl]amino]-2-oxohexanoyl-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN D-Phenylalanine, N-[(1,1-dimethylethoxy)carbonyl]-L-.alpha.-aspartyl-L-prolyl-N6-[imino(nitroamino)methyl]-2-oxo-(S)-3,6-diaminohexanoyl-, bis(phenylmethyl) ester
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C44 H54 N8 O12
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

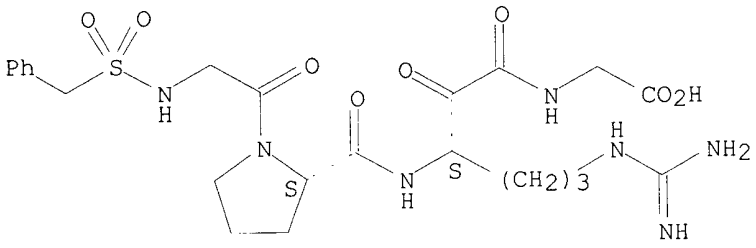
REFERENCE 1: 126:199831

REFERENCE 2: 122:56583

L12 ANSWER 23 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **159945-55-8** REGISTRY
CN Glycine, N-[(phenylmethyl)sulfonyl]glycyl-L-prolyl-(3S)-3-amino-6-[(aminoiminomethyl)amino]-2-oxohexanoyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glycine, N-[(phenylmethyl)sulfonyl]glycyl-L-prolyl-N6-(aminoiminomethyl)-2-oxo-(S)-3,6-diaminohexanoyl-
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C23 H33 N7 O8 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 126:199831

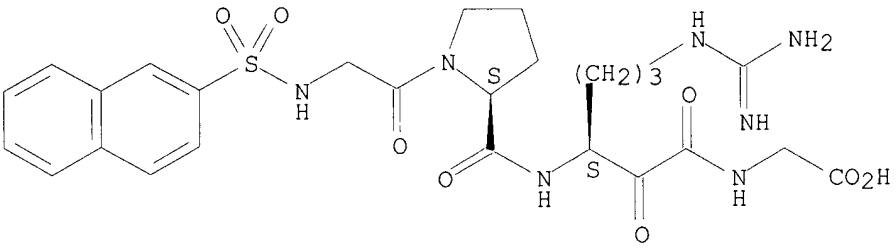
REFERENCE 2: 122:56583

L12 ANSWER 24 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **159945-54-7** REGISTRY
CN Glycine, N-(2-naphthalenylsulfonyl)glycyl-L-prolyl-(3S)-3-amino-6-[(aminoiminomethyl)amino]-2-oxohexanoyl- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:
CN Glycine, N-(2-naphthalenylsulfonyl)glycyl-L-prolyl-N6-(aminoiminomethyl)-2-oxo-(S)-3,6-diaminohexanoyl-
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C26 H33 N7 O8 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

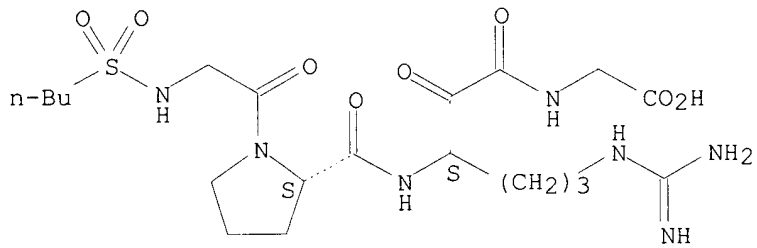
REFERENCE 1: 126:199831

REFERENCE 2: 122:56583

L12 ANSWER 25 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **159945-53-6** REGISTRY
CN Glycine, N-(butylsulfonyl)glycyl-L-prolyl-(3S)-3-amino-6-[(aminoiminomethyl)amino]-2-oxohexanoyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glycine, N-(butylsulfonyl)glycyl-L-prolyl-N6-(aminoiminomethyl)-2-oxo-(S)-3,6-diaminohexanoyl-
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C20 H35 N7 O8 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

Absolute stereochemistry.



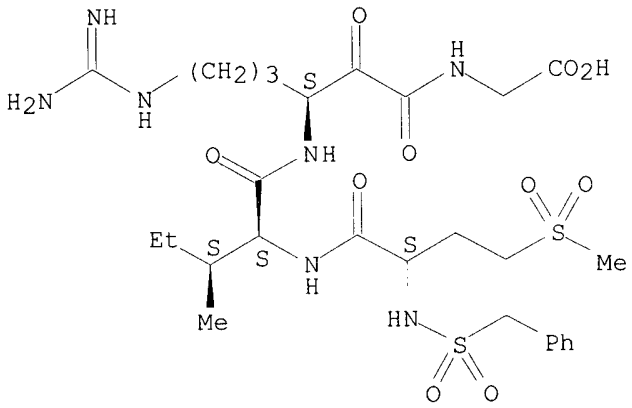
2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 126:199831

REFERENCE 2: 122:56583

L12 ANSWER 26 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **159945-50-3** REGISTRY
CN Glycine, (2S)-4-(methylsulfonyl)-2-[[(phenylmethyl)sulfonyl]amino]butanoyl-L-isoleucyl-(3S)-3-amino-6-[(aminoiminomethyl)amino]-2-oxohexanoyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glycine, 4-(methylsulfonyl)-N-[(phenylmethyl)sulfonyl]-L-2-aminobutanoyl-L-isoleucyl-N6-(aminoiminomethyl)-2-oxo-(S)-3,6-diaminohexanoyl-
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C27 H43 N7 O10 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

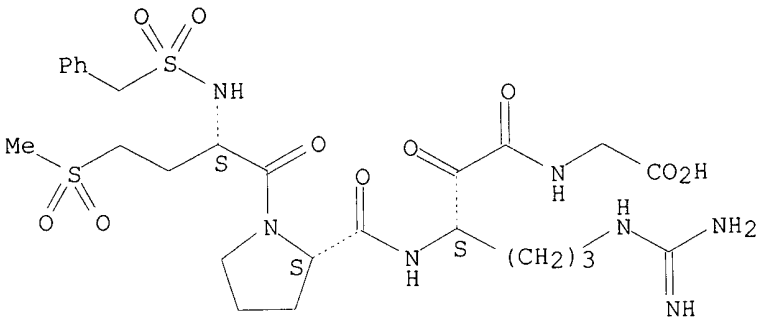
REFERENCE 1: 126:199831

REFERENCE 2: 122:56583

L12 ANSWER 27 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **159945-43-4** REGISTRY
CN Glycine, (2S)-4-(methylsulfonyl)-2-[[(phenylmethyl)sulfonyl]amino]butanoyl-L-prolyl-(3S)-3-amino-6-[(aminoiminomethyl)amino]-2-oxohexanoyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glycine, 4-(methylsulfonyl)-N-[(phenylmethyl)sulfonyl]-L-2-aminobutanoyl-L-prolyl-N6-(aminoiminomethyl)-2-oxo-(S)-3,6-diaminohexanoyl-
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C26 H39 N7 O10 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

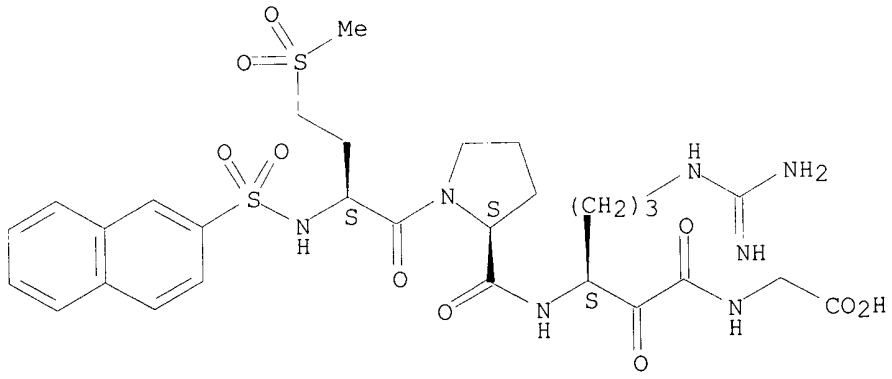
REFERENCE 1: 126:199831

REFERENCE 2: 122:56583

L12 ANSWER 28 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **159945-42-3** REGISTRY
CN Glycine, (2S)-4-(methylsulfonyl)-2-[(2-naphthalenylsulfonyl)amino]butanoyl-L-prolyl-(3S)-3-amino-6-[(aminoiminomethyl)amino]-2-oxohexanoyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glycine, 4-(methylsulfonyl)-N-(2-naphthalenylsulfonyl)-L-2-aminobutanoyl-L-prolyl-N6-(aminoiminomethyl)-2-oxo-(S)-3,6-diaminohexanoyl-
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C29 H39 N7 O10 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

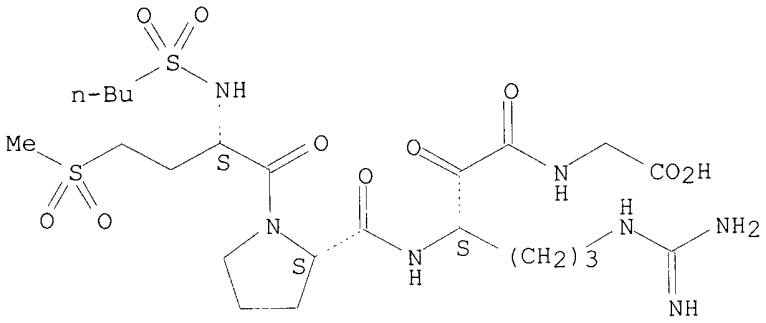
REFERENCE 1: 126:199831

REFERENCE 2: 122:56583

L12 ANSWER 29 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **159945-41-2** REGISTRY
CN Glycine, (2S)-2-[(butylsulfonyl)amino]-4-(methylsulfonyl)butanoyl-L-prolyl-(3S)-3-amino-6-[(aminoiminomethyl)amino]-2-oxohexanoyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glycine, N-(butylsulfonyl)-4-(methylsulfonyl)-L-2-aminobutanoyl-L-prolyl-N6-(aminoiminomethyl)-2-oxo-(S)-3,6-diaminohexanoyl-
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C23 H41 N7 O10 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

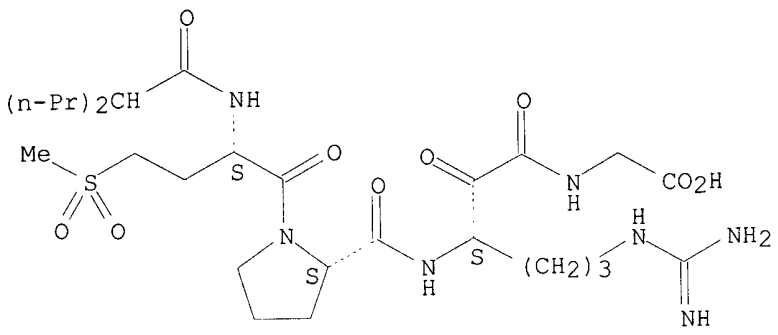
REFERENCE 1: 126:199831

REFERENCE 2: 122:56583

L12 ANSWER 30 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **159945-38-7** REGISTRY
CN Glycine, 4-(methylsulfonyl)-N-(1-oxo-2-propylpentyl)-L-2-aminobutanoyl-L-prolyl-N6-(aminoiminomethyl)-2-oxo-(S)-3,6-diaminohexanoyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C27 H47 N7 O9 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

Absolute stereochemistry.

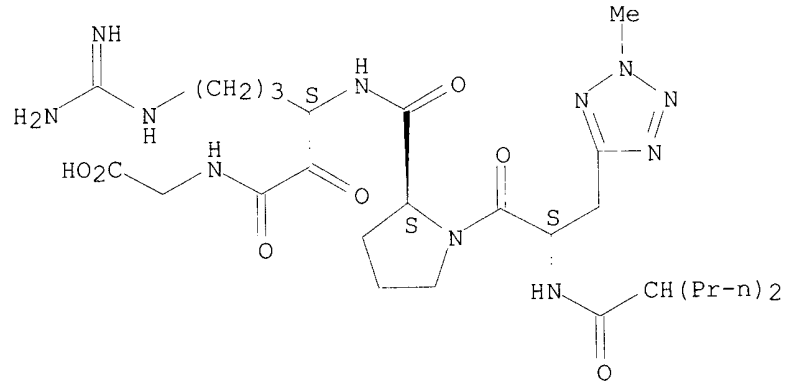


1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 122:56583

L12 ANSWER 31 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **159945-35-4** REGISTRY
CN Glycine, 3-(2-methyl-2H-tetrazol-5-yl)-N-(1-oxo-2-propylpentyl)-L-alanyl-L-prolyl-N6-(aminoiminomethyl)-2-oxo-(S)-3,6-diaminohexanoyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C27 H45 N11 O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

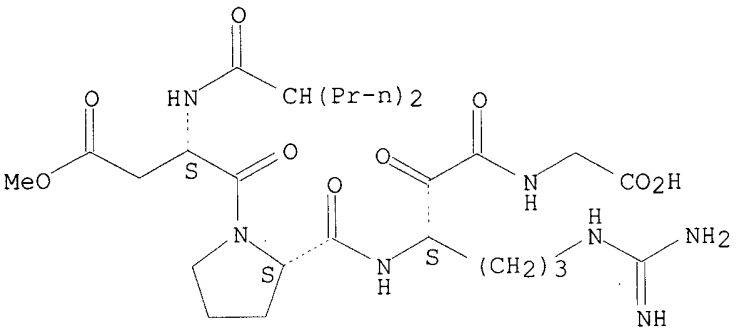


1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 122:56583

L12 ANSWER 32 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **159945-32-1** REGISTRY
CN Glycine, N-(1-oxo-2-propylpentyl)-L-.alpha.-aspartyl-L-prolyl-N6-(aminoiminomethyl)-2-oxo-(S)-3,6-diaminohexanoyl-, 4-methyl ester (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C27 H45 N7 O9
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

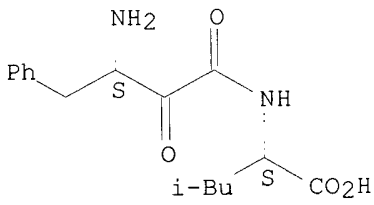


1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 122:56583

L12 ANSWER 33 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **142699-25-0** REGISTRY
CN L-Leucine, N-(3-amino-1,2-dioxo-4-phenylbutyl)-, (S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C16 H22 N2 O4
CI COM
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 117:85791

L12 ANSWER 34 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **78990-62-2** REGISTRY
CN Calpain (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Calcium-activated neutral protease
CN Calcium-activated neutral proteinase
CN Calcium-dependent neutral protease
CN Calpain p94
CN E.C. 3.4.22.17
CN Proteinase, calcium-activated neutral
MF Unspecified
CI MAN
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA,

CAPLUS, CEN, CHEMCATS, CIN, EMBASE, IPA, PROMT, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
2754 REFERENCES IN FILE CA (1962 TO DATE)
14 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2768 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:308575

REFERENCE 2: 137:306900

REFERENCE 3: 137:305778

REFERENCE 4: 137:305774

REFERENCE 5: 137:304817

REFERENCE 6: 137:304520

REFERENCE 7: 137:293340

REFERENCE 8: 137:292185

REFERENCE 9: 137:292016

REFERENCE 10: 137:289602

L12 ANSWER 35 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **60616-82-2** REGISTRY
CN Cathepsin L (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Aldrichina grahami cysteine proteinase
CN Cathepsin L1
CN Cathepsin L2
CN E.C. 3.4.22.15
CN Pacific whiting surimi wash water proteinase
MF Unspecified
CI MAN
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CHEMCATS, CIN, EMBASE, PROMT, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1517 REFERENCES IN FILE CA (1962 TO DATE)
12 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1519 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:309392

REFERENCE 2: 137:308852

REFERENCE 3: 137:308379

REFERENCE 4: 137:292545

REFERENCE 5: 137:291871

REFERENCE 6: 137:260870

REFERENCE 7: 137:259547

REFERENCE 8: 137:247932

REFERENCE 9: 137:230356

REFERENCE 10: 137:230348

L12 ANSWER 36 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **37353-41-6** REGISTRY
CN Proteinase, cysteine (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Cysteine endopeptidase
CN Cysteine endoprotease
CN Cysteine peptidase
CN Cysteine protease
CN Cysteine proteinase
CN L-Cysteine proteinase
CN Mercapto proteinase
CN Oryzain
CN Papain-like cysteine protease
CN Sulfhydryl endopeptidase
CN Sulfhydryl esterase
CN Sulfhydryl protease
CN Sulfhydryl proteinase
CN Thiol endopeptidase
CN Thiol endoproteinase
CN Thiol protease
CN Thiol proteinase
CN Thioprotease
CN Trigger peptidase
DR 51484-59-4, 116155-86-3, 116412-41-0, 117990-23-5
MF Unspecified
CI MAN
LC STN Files: ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CEN, CIN, EMBASE, MEDLINE, PROMT, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
3119 REFERENCES IN FILE CA (1962 TO DATE)
30 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3123 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:311203

REFERENCE 2: 137:306641

REFERENCE 3: 137:306631

REFERENCE 4: 137:299872

REFERENCE 5: 137:295246

REFERENCE 6: 137:294304

REFERENCE 7: 137:291866

REFERENCE 8: 137:289678

REFERENCE 9: 137:289669

REFERENCE 10: 137:288591

L12 ANSWER 37 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **37259-58-8** REGISTRY
CN Proteinase, serine (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Bacillus alk. serine proteinase

CN Bactosol SI
CN Caldolase
CN Cerastobin
CN Gene easter serine protease
CN Herpes simplex virus type 1 proteinase
CN Proteinase R
CN Proteinase T
CN Proteins, gene easter
CN Proteins, gene snake
CN Prozyme 6
CN Serine endopeptidase
CN Serine esterase
CN Serine peptidase
CN Serine protease
CN Serine proteinase
CN Serine-type protease
CN Seryl protease
CN Tryase
DR 139074-63-8, 116036-72-7
MF Unspecified
CI MAN
LC STN Files: ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST, CIN, EMBASE, IFICDB, IFIPAT, IFIUDB, PROMT, RTECS*, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
5644 REFERENCES IN FILE CA (1962 TO DATE)
82 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5656 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:309165

REFERENCE 2: 137:307554

REFERENCE 3: 137:306604

REFERENCE 4: 137:306479

REFERENCE 5: 137:304523

REFERENCE 6: 137:299886

REFERENCE 7: 137:294304

REFERENCE 8: 137:291688

REFERENCE 9: 137:290814

REFERENCE 10: 137:290366

L12 ANSWER 38 OF 38 REGISTRY COPYRIGHT 2002 ACS
RN **9001-92-7** REGISTRY
CN Proteinase (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 537 Acidic protease
CN Actinase
CN Alkalase 2.4L FG
CN Alkalase 2.5L Type DX
CN Alkaline protease-L FG
CN ALP 901

CN AO protease
CN APL 901
CN Aquatinase E
CN Arginine esterase
CN AS 1.398
CN AS 10
CN Azocaseinase
CN BAPAase
CN Bioprase SP-4FG
CN Bioprotease A
CN Bioprotease N 100P
CN Carbonyl hydrolase
CN Casein endopeptidase
CN Caseinase
CN Cleanase AP 100-PWC
CN Corolase 7089
CN Corolase L 10
CN DA 10
CN DA 10 (enzyme)
CN Denatyme AP
CN Durazyme 16.0L
CN Endopeptidase
CN Endopeptidase O
CN Endoprotease
CN Endoproteinase
CN Enzylase K 40
CN Enzylon SAL
CN Enzylon SAL 300
CN Enzymes, proteolytic
CN Esteroproteinase
CN Everlase 16L
CN Everlase 16L Type EX
CN Fibrinase
CN Flavourzyme 500 MG
CN Fungal Protease P 31000
CN Genencor 4000 S
CN GHPO 525 protease
CN GPR protease
CN Growth-related proteinase
CN HAP Alkaline protease
CN Isofloridoside phosphate synthase-activating proteinase
CN Kanase 12T
CN Kanase 24T
CN KAP 11.1G
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
DR 9001-93-8, 9012-23-1, 9040-76-0, 125498-72-8, 125752-86-5, 123779-18-0, 124041-97-0, 120038-39-3, 120038-40-6, 105913-13-1, 118901-82-9, 144906-30-9, 143404-30-2, 143404-41-5, 116267-38-0, 117278-03-2, 117698-27-8, 118390-80-0
MF Unspecified
CI COM, MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MSDS-OHS, NAPRALERT, NIOSHTIC, PIRA, PLASPEC*, PROMT, RTECS*, TOXCENTER, TULSA, USPAT2, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
34229 REFERENCES IN FILE CA (1962 TO DATE)

390 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
34276 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:316147

REFERENCE 2: 137:315949

REFERENCE 3: 137:313019

REFERENCE 4: 137:312741

REFERENCE 5: 137:311153

REFERENCE 6: 137:310022

REFERENCE 7: 137:310021

REFERENCE 8: 137:309947

REFERENCE 9: 137:309939

REFERENCE 10: 137:309917

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=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 09:46:38 ON 18 NOV 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 18 Nov 2002  VOL 137 ISS 21
FILE LAST UPDATED: 17 Nov 2002  (20021117/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

=>
=>

=> d stat que l13 nos
L1              STR
L3          1987 SEA FILE=REGISTRY SSS FUL L1
L4              STR
L5          1955 SEA FILE=REGISTRY SUB=L3 SSS FUL L4
L6            68 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5
L7            44 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L6 AND PD<DECEMBER 3 1999
L8         17584 SEA FILE=REGISTRY ABB=ON  PLU=ON  PROTEASE? OR PROTEINASE?
L9        173122 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8 OR PROTEASE? OR PROTEINASE?

L10           24 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND L7
L11            7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 AND ?KETOAMI?
L13           17 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 NOT L11


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L13  ANSWER 1 OF 17  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         1998:485077  HCAPLUS
DOCUMENT NUMBER:          129:122872
TITLE:                    Peptidomimetic inhibitors of the human cytomegalovirus
                          protease
INVENTOR(S):              Bailey, Murray; Fazal, Gulrez; Lavallee, Pierre;
                          Ogilvie, William; Poupart, Marc-Andre
PATENT ASSIGNEE(S):       Boehringer Ingelheim (Canada) Ltd., Can.
SOURCE:                   PCT Int. Appl., 165 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:
```

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9829435 | A1 | 19980709 | WO 1997-CA1004 | 19971223 <-- |
| W: CA, JP, MX, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| EP 948523 | A1 | 19991013 | EP 1997-951048 | 19971223 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2001508418 | T2 | 20010626 | JP 1998-529511 | 19971223 |
| US 6291640 | B1 | 20010918 | US 1998-171554 | 19981019 |

PRIORITY APPLN. INFO.:
US 1996-34041P P 19961227
US 1997-52860P P 19970717
US 1997-59806P P 19970923
WO 1997-CA1004 W 19971223

OTHER SOURCE(S): MARPAT 129:122872

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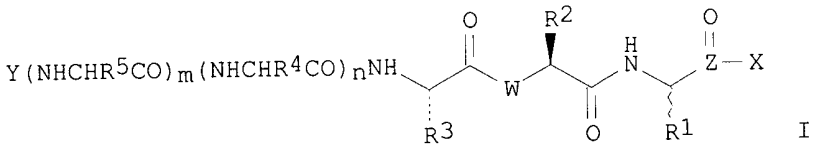



I

AB Compds. I [Z = C or P; X = CF3, C2F5, benzothiazole, CF2CONHR6, CONHR6 [R6 = alkyl, (un)substituted Ph or cyclohexyl], etc.; R1 = H, Me, Et; R2 = CH2SO2NH2, alkyl, arylalkyl, etc.; R3 = alkyl, carboxyalkyl, adamantyl; R4 = alkyl, arylalkyl; R5 = H, CH2OH; W = NH, CH2, CHMe; Y = H, t-BuCH2CH2, acyl; m, n = 0, 1] were prepd. as inhibitors of the human cytomegalovirus (HCMV) **protease**. Thus, N1-(3,3,3-trifluoro-1-methyl-2-oxopropyl)-(2S)-2-[(1S)-2-methyl-1-[[(1S)-2-methyl-1-[(methylcarboxamido)methyl]carboxamidopropyl]carboxamido]propylcarboxamido]butanediamide, prepd. by the solid-phase method, showed IC50 = 1.8.+-.0.3 .mu.M for inhibition of HCMV No **protease**.

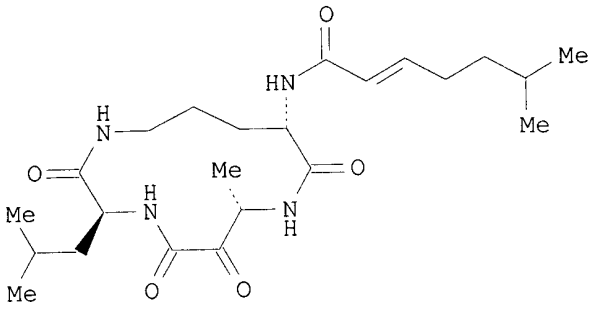
IT **210290-94-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptidomimetic inhibitors of the human cytomegalovirus **protease**)

IT **139691-88-6**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(peptidomimetic inhibitors of the human cytomegalovirus **protease**)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 17 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:26310 HCAPLUS
DOCUMENT NUMBER: 128:35014
TITLE: Synthesis of the Cyclic Peptidic **Protease** Inhibitor Eurystatin A Using Acyl Cyano Phosphorane Methodology
AUTHOR(S): Wasserman, Harry H.; Petersen, Anders K.
CORPORATE SOURCE: Department of Chemistry, Yale University, New Haven, CT, 06520-8107, USA
SOURCE: Journal of Organic Chemistry (**1997**), 62(26), 8972-8973
CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 128:35014
GI



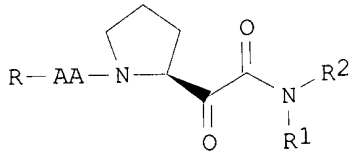
I

AB A synthesis of the cyclic **protease** inhibitor eurystatin A (I) was accomplished by two different routes, involving .alpha.,.beta.-diketo nitriles obtained by oxidn. of the corresponding acyl cyano phosphoranes. Coupling with leucine tert-Bu ester furnished the key .alpha.-keto amide functionality found in the natural product.

IT **199467-17-9P 199467-18-0P 199467-19-1P 199467-27-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of cyclopeptide **protease** inhibitor eurystatin A using acyl cyano phosphorane methodol.)

IT **199467-13-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of cyclopeptide **protease** inhibitor eurystatin A using acyl cyano phosphorane methodol.)

L13 ANSWER 3 OF 17 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:592182 HCAPLUS
DOCUMENT NUMBER: 125:301555
TITLE: Poststatin, a new inhibitor of prolyl endopeptidase. VII. N-cycloalkylamide analogs
AUTHOR(S): Tsuda, Makoto; Muraoka, Yasuhiko; Nagai, Machiko; Aoyagi, Takaaki; Takeuchi, Tomio
CORPORATE SOURCE: Inst. Microbial Chem., Tokyo, 141, Japan
SOURCE: Journal of Antibiotics (**1996**), 49(9), 909-920
CODEN: JANTAJ; ISSN: 0021-8820
PUBLISHER: Japan Antibiotics Research Association
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Poststatin analogs I [R = Me3CO2C (Boc), Ac, 4-ClC6H4CH2NH, PhCH2O2C (Z), 2-thienylcarbonyl, 3-PhOC6H4CO, 2-naphthylcarbonyl, 2-quinolinecarbonyl, 2-pyridinecarbonyl, 3-(2-furyl)propenoyl, 3-cyclohexylpropanoyl; AA = COCH2CH2CO, Phe, Val, 3-cyclohexylalanine (Cha); R1 = H, R2 = cyclopropyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl; R1R2 = (CH2)4] contg. oxo(pyrrolidinyl)acetyl moieties in the P1 positions were prepd. and examd. for their inhibitory activity against prolyl endopeptidase and cathepsin B in vitro. Introduction of nonpeptidyl cycloalkylamine components in P'1 was effective and P3-acyl groups must be widely modifiable for prolyl endopeptidase inhibition. Compds. I (AA = Phe) showed IC50 value of nano to subnano g/mL as prolyl endopeptidase inhibitors and show no significant inhibitory activities against cathepsin B, a cysteine **protease**.

IT **135219-43-1DP**, Poststatin, cycloalkylamide analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of poststatin cycloalkylamide analogs as prolyl endopeptidase inhibitors)

IT **72162-84-6**, Prolyl endopeptidase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prepn. of poststatin cycloalkylamide analogs as prolyl endopeptidase inhibitors)

L13 ANSWER 4 OF 17 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:592180 HCAPLUS
DOCUMENT NUMBER: 125:301554
TITLE: Poststatin, a new inhibitor of prolyl endopeptidase. V. Endopeptidase inhibitory activity of poststatin analogs
AUTHOR(S): Tsuda, Makoto; Muraoka, Yasuhiko; Nagal, Machiko; Aoyagi, Takaaki; Takeuchi, Tomio
CORPORATE SOURCE: Inst. Microbial Chem., Tokyo, 141, Japan
SOURCE: Journal of Antibiotics (**1996**), 49(9), 890-899
CODEN: JANTAJ; ISSN: 0021-8820
PUBLISHER: Japan Antibiotics Research Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Thirty analogs of poststatin were synthesized, and their inhibitory activities against prolyl endopeptidase, human leukocyte elastase and cathepsin B were measured. In the .beta.-substituted-.beta.-amino-.alpha.-oxopropionic acid moiety of poststatin analogs, the .alpha.-keto group was essential and the S stereo configuration was more preferable than R for endopeptidase inhibitory activity. The analog in which the D-leucine residue of poststatin was replaced by L-leucine showed strong inhibitory activity to cathepsin B. Introduction of an arom. group into the P4 position and proline into the P2 position increased inhibitory activity to elastase. Benzyloxycarbonyl-L-homophenylalanyl-(RS)-3-amino-2-oxovaleryl-D-leucyl-L-valine was about 6 times more active to prolyl endopeptidase than natural poststatin.

IT **9004-06-2**, Elastase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(human leukocyte; prepn. of poststatin analogs and study of their endopeptidase inhibitory activities)

IT **135219-43-1D**, Poststatin, analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of poststatin analogs and study of their endopeptidase inhibitory activities)

IT **135219-45-3P 135219-46-4P 135219-48-6P**

**135219-49-7P 135219-50-0P 135219-52-2P**
**135219-53-3P 135219-54-4P 135219-55-5P**
**135219-56-6P 135219-57-7P 135219-58-8P**
**135219-62-4P 135270-54-1P 135355-22-5P**
**141187-11-3P 182742-35-4P 182742-36-5P**
**182742-38-7P 182742-39-8P 182742-40-1P**
**182742-41-2P 182742-42-3P 182966-18-3P**
**182966-19-4P 182966-20-7P 182966-21-8P**
**182966-22-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of poststatin analogs and study of their endopeptidase inhibitory activities)

IT **72162-84-6**, Prolyl endopeptidase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prepn. of poststatin analogs and study of their endopeptidase inhibitory activities)

L13 ANSWER 5 OF 17 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:108206 HCAPLUS
DOCUMENT NUMBER: 124:250214
TITLE: Comparison of sustained antithrombotic effects of inhibitors of thrombin and factor Xa in experimental thrombosis
AUTHOR(S): Biemond, Bart J.; Friederich, Philip W.; Levi, Marcel; Vlasuk, George P.; Buller, Harry R.; ten Cate, Jan W.
CORPORATE SOURCE: Center Hemostasis Thrombosis Atherosclerosis and Inflammation Research, Academic Medical Center, Amsterdam, 1105 AZ, Neth.
SOURCE: Circulation (**1996**), 93(1), 153-60
CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: American Heart Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the pathogenesis of (recurrent) thrombosis, clot-assocd. thrombin appears to play an important role. Antithrombin III-independent thrombin inhibitors have been shown to neutralize clot-bound thrombin effectively. We compared the sustained antithrombotic effects and the effects on endogenous fibrinolysis of several of these agents with recombinant anticoagulant peptide (rTAP), a selective factor Xa inhibitor, and low-mol.-wt. heparin (LMWH) in an exptl. venous thrombosis model. Rabbits received either recombinant hirudin (rHir), Hirulog-1, CVS#995 (a novel direct inhibitor of thrombin), rTAP, LMWH, or saline. The effect on thrombus growth was assessed by measuring the accretion of 125I-labeled fibrinogen onto preformed nonradioactive thrombi, and the effect on endogenous fibrinolysis was assessed by measuring the decline in radioactivity of preformed 125I-labeled thrombi in rabbit jugular veins. All direct thrombin inhibitors induced a sustained antithrombotic effect compared with either LMWH and rTAP. In addn., CVS#995 also further decreased thrombus size after stopping its infusion, which was due to a significant enhancement of endogenous fibrinolysis. Direct thrombin inhibition by rHir, Hirulog-1, or CVS#995 induces a sustained antithrombotic effect compared with rTAP and LMWH, which is most likely due to inhibition of clot-bound thrombin. CVS#995 was shown to also enhance the extent of endogenous fibrinolysis to a greater degree compared with rHir and might therefore be an interesting new antithrombotic agent for the treatment of venous and arterial thrombosis.

IT **129737-17-3**, Tick anticoagulant peptide **166247-65-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(comparison of sustained antithrombotic effects of inhibitors of thrombin and factor Xa in exptl. thrombosis)

L13 ANSWER 6 OF 17 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:700707 HCAPLUS
DOCUMENT NUMBER: 123:106201
TITLE: Inhibitors of human heart chymase based on a peptide library
AUTHOR(S): Bastos, Margarita; Maeji, N. Joe; Abeles, Robert H.
CORPORATE SOURCE: Dep. Biochemistry, Brandeis Univ., Waltham, MA, 02254, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (**1995**), 92(15), 6738-42
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have synthesized two sets of noncleavable peptide-inhibitor libraries to map the S and S' subsites of human heart chymase. Human heart chymase is a chymotrypsin-like enzyme that converts angiotensin I to angiotensin II. The first library consists of peptides with 3-fluorobenzylpyruvamides in the P1 position. (Amino acid residues of substrates numbered P1, P2, etc., are toward the N-terminal direction, and P1', P2', etc., are toward the C-terminal direction from the scissile bond.). The P1' and P2' positions were varied to contain each one of the 20 naturally occurring amino acids and P3' was kept const. as an arginine. The second library consists of peptides with phenylalanine keto-amides at P1, glycine in P1', and benzyloxycarbonyl (Z)-isoleucine in P4. The P2 and P3 positions were varied to contain each of the naturally occurring amino acids, except for cysteine and methionine. The peptides of both libraries are attached to a solid support (pins). The peptides are evaluated by immersing the pins in a soln. of the target enzyme and evaluating the amt. of enzyme absorbed. The pins with the best inhibitors will absorb most enzyme. The libraries select the best and worst inhibitors within each group of peptides and provide an approx. ranking of the remaining peptides according to Ki. Through this library, the authors detd. that Z-Ile-Glu-Pro-Phe-CO2Me and (F)-Phe-CO-Glu-Asp-ArgOMe should be the best inhibitors of chymase in this collection of peptide inhibitors. The authors synthesized the peptides and found Ki values were 1 nM and 1 .mu.M, resp. The corresponding Ki values for chymotrypsin were 10 nM and 100 .mu.M. The use of libraries of inhibitors has advantages over the classical method of synthesis of potential inhibitors in soln.: the libraries are reusable, the same libraries can be used with a variety of different serine **proteases**, and the method allows the screening of hundreds of compds. in short periods of time.

IT **37259-58-8**, Serine **protease** **97501-92-3**, Chymase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibitors of human heart chymase based on a peptide library)

IT **166267-80-7P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(inhibitors of human heart chymase based on a peptide library)

L13 ANSWER 7 OF 17 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:440143 HCAPLUS
DOCUMENT NUMBER: 123:112687
TITLE: Synthesis and human immunodeficiency virus (HIV)-1 **protease** inhibitory activity of tripeptide

analogs containing a dioxoethylene moiety

AUTHOR(S): Kitazaki, Tomoyuki; Asano, Tsuneo; Kato, Koichi; Kishimoto, Shoji; Itoh, Katsumi

CORPORATE SOURCE: Pharmaceutical Research Laboratories III, Takeda Chemical Industries, Ltd., Osaka, 532, Japan

SOURCE: Chemical & Pharmaceutical Bulletin (**1994**), 42(12), 2636-40
CODEN: CPBTAL; ISSN: 0009-2363

PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

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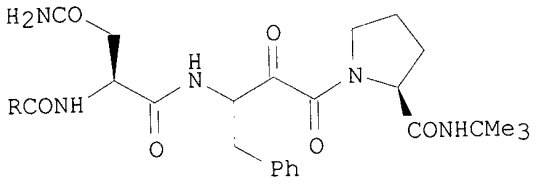


I

AB Tripeptide analogs I (R = PhCH2O, 2-quinolyl), contg. a dioxoethylene moiety, were designed based on the characteristic structure of the naturally occurring human immunodeficiency virus (HIV)-1 **protease** inhibitors RPI-856 A, B, C and D. I showed high inhibitory activity, comparable to that of RPI-856 A, against HIV-1 **protease** in vitro.

IT **9001-92-7, Protease**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(human immunodeficiency virus-1; synthesis and human immunodeficiency virus-1 **protease** inhibitory activity of tripeptide analogs contg. a dioxoethylene moiety)

IT **157341-54-3 157381-54-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis and human immunodeficiency virus-1 **protease** inhibitory activity of tripeptide analogs contg. a dioxoethylene moiety)

L13 ANSWER 8 OF 17 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:227654 HCAPLUS
DOCUMENT NUMBER: 122:131140
TITLE: Poststatin and related compounds or salts thereof
INVENTOR(S): Takeuchi, Tomio; Aoyagi, Takaaki; Hamada, Masa; Naganawa, Hiroshi; Ogawa, Keiji; Nagai, Machiko; Muraoka, Yasuhiko; Tsuda, Makoto
PATENT ASSIGNEE(S): Zaidan Hojin Biseibutsu Kagaku Kenkyu KaI, Japan
SOURCE: U.S., 20 pp. Cont.-in-part of U.S. 5,162,500.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5359138 | A | 19941025 | US 1992-905792 | 19920629 <-- |

| | | | | |
|---|---|---|---|---|
| EP 672648 | A1 | 19950920 | EP 1995-106762 | 19900413 <-- |
| EP 672648 | B1 | 19980923 | | |
| R: DE, FR, GB, IT | | | | |
| US 5162500 | A | 19921110 | US 1990-613759 | 19901207 <-- |
| PRIORITY APPLN. INFO.: | | | JP 1989-94328 | 19890415 |
| | | | US 1990-613759 | 19901207 |
| | | | EP 1990-905686 | 19900413 |
| | | | WO 1990-JP491 | 19900413 |

OTHER SOURCE(S): MARPAT 122:131140

AB A novel, biol. active substance, poststatin, was isolated from a culture medium of Streptomyces. The novel substance is a peptide compd. having a novel structure, wherein the peptide chains have ketone radicals. Thus the substance has a high endopeptidase inhibition activity. It is possible to chem. synthesize poststatin-related compds. having ketone radicals in the peptide chains. These compds. also have endopeptidase inhibition activity.

IT **135219-44-2P 135219-46-4P 135219-48-6P**
**135219-49-7P 135219-50-0P 135219-51-1P**
**135219-52-2P 135219-53-3P 135219-54-4P**
**135219-55-5P 135219-56-6P 135219-57-7P**
**135219-58-8P 135219-59-9P 135219-60-2P**
**135219-61-3P 135219-62-4P 135270-54-1P**
**135355-22-5P 141187-11-3P 141187-12-4P**
**141187-13-5P 141187-14-6P 141187-15-7P**
**160772-54-3P 160772-55-4P 160866-54-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(endopeptidase inhibiting poststatin deriv.)

IT **135219-43-1P**, Poststatin
RL: BAC (Biological activity or effector, except adverse); BMF (Bioindustrial manufacture); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(endopeptidase inhibitor poststatin from Streptomyces viridochromonogenes)

IT **37205-61-1**, **Proteinase** inhibitor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(endopeptidase inhibitor poststatin from Streptomyces viridochromonogenes)

IT **72162-84-6**, Prolylendopeptidase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; endopeptidase inhibitor poststatin from Streptomyces viridochromonogenes)

L13 ANSWER 9 OF 17 HCAPLUS COPYRIGHT 2002 ACS

| | |
|---|---|
| ACCESSION NUMBER: | 1995:31017 HCAPLUS |
| DOCUMENT NUMBER: | 122:133766 |
| TITLE: | Stereospecific Synthesis of Peptidyl .alpha.-Keto Amides as Inhibitors of Calpain |
| AUTHOR(S): | Harbeson, Scott L.; Abelleira, Susan M.; Akiyama, Alan; Barrett, Robert, III; Carroll, Renee M.; Straub, Julie Ann; Tkacz, Jaroslaw N.; Wu, Chichih; Musso, Gary F. |
| CORPORATE SOURCE: | Alkermes Inc., Cambridge, MD, 02139-4136, USA |
| SOURCE: | Journal of Medicinal Chemistry (**1994**), 37(18), 2918-29<br>CODEN: JMCMAR; ISSN: 0022-2623 |
| DOCUMENT TYPE: | Journal |
| LANGUAGE: | English |

AB Peptidyl .alpha.-keto amides have been synthesized and tested as inhibitors of the cysteine **protease** calpain. A stereospecific synthesis was devised in which protected dipeptidyl .alpha.-hydroxy amides

were oxidized with TEMPO/hypochlorite to the corresponding .alpha.-keto amides. This oxidn. was accomplished in good yields and without epimerization of the chiral center adjacent to the ketone. The potent inhibition of porcine calpain I by the L,L diastereomers, combined with the poor inhibition by the L,D diastereomers, established the requirement for the all-L stereochem. of the active inhibitor. The early lead inhibitors were very hydrophobic and, therefore, poorly sol. in aq. solns. Using the stereospecific route, new compds. were prepd. with polar groups at the C- and N-termini. These modifications resulted in more sol. inhibitors that were still potent inhibitors of calpain. Studies of the stability of these .alpha.-keto amides showed that abs. stereochem. can be maintained in acidic and unbuffered environments but general base-catalyzed epimerization of the chiral center adjacent to the ketone occurred rapidly. The .alpha.-hydroxy precursors were inactive as inhibitors of calpain, which supports the hypothesis that the .alpha.-keto compds. reversibly form an enzyme-bound tetrahedral species that results from the nucleophilic addn. of the catalytic thiol of calpain to the electrophilic ketone of the inhibitor.

IT **78990-62-2**, Calpain
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pig calpain I; stereospecific synthesis of peptidyl .alpha.-keto amides as inhibitors of calpain)

IT **160801-90-1P 160801-92-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(stereospecific synthesis of peptidyl .alpha.-keto amides as inhibitors of calpain)

L13 ANSWER 10 OF 17 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:650735 HCAPLUS
DOCUMENT NUMBER: 121:250735
TITLE: Novel retrovirus **protease** inhibitors, RPI-856 A, B, C, and D, produced by Streptomyces sp. AL-322
AUTHOR(S): Asano, Tsuneo; Matsuoka, Kunio; Hida, Tsuneaki; Kobayashi, Makoto; Kitamura, Yumiko; Hayakawa, Takaki; Iinuma, Shigemi; Kakinuma, Atsushi; Kato, Koichi
CORPORATE SOURCE: Discovery Res. Div., Takeda Chem. Ind., Ltd., Osaka, 532, Japan
SOURCE: Journal of Antibiotics (**1994**), 47(5), 557-65
CODEN: JANTAJ; ISSN: 0021-8820
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Four kinds of retrovirus **protease** (retropepsin) inhibitors (RPI-856 A, B, C, and D) were isolated as white powder from the culture filtrate of a soil isolate, Streptomyces sp. AL-322 by column chromatog. using Diaion HP-20, Sephadex LH-20, ODS reversed phase HPLC and SP-2SW ion-exchange HPLC. The structures of these inhibitors were elucidated by physicochem. properties, chem. reactions and spectral anal., as valyl-ADPAA-leucyl-AOPBA-valyl-valyl-aspartic acid (RPI-856 A and B) and valyl-ADPAA-leucyl-AOPBA-valyl-valine (RPI-856 C and D) [ADPAA = 2-amino-2-(3,5-dihydroxyphenyl)acetic acid, AOPBA = 3-amino-2-oxo-4-phenylbutyric acid]. RPI-856 A and B, and RPI-856 C and D were both detd. to be diastereomers to each other on the asym. C in AOPBA. These 4 inhibitors strongly inhibited in vitro HIV-1 and HTLV-1 retropepsins, both derived from recombinant Escherichia coli with IC50 of 10-7-10-8 M.

IT **157381-54-9 157381-55-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(as retropepsin inhibitor from Streptomyces, isolation and characterization and redn. of)

IT **144114-21-6**, Retropepsin

RL: PROC (Process)
(inhibition of, of HIV-1 virus, by aminooxophenylbutyrate-contg. peptides from Streptomyces)

IT **157341-54-3 157341-55-4**
RL: BIOL (Biological study)
(retroviral **protease** inhibitor, from Streptomyces)

L13 ANSWER 11 OF 17 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:573417 HCAPLUS
DOCUMENT NUMBER: 119:173417
TITLE: Prolyl endopeptidase inhibitors
AUTHOR(S): Aoyagi, Takaaki; Muraoka, Yasuhiko
CORPORATE SOURCE: Showa Coll. Pharm. Sci., Machida, 194, Japan
SOURCE: Tanpakushitsu Kakusan Koso (**1993**), 38(11), 1971-86
CODEN: TAKKAJ; ISSN: 0039-9450
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review with 81 refs. on prolyl endopeptidase (PEP) and its inhibitors, poststatins. It had been found that PEP activity was increased in spleen of systemic lupus erythematosus model animal and brain tissue of Alzheimer's disease (AD). Properties of PEP, gradual changes of enzyme activity in spleen of control mouse DBA/Z and hybrid mouse NZB/W, correlation between PEP activity and Pro-IP activity in each organ or in spleen are described. Changes in brain or in serum **protease** activity of AD are also described. Structure and activity of postatin, an inhibitor of PEP isolated from S. viridochromogenes, and its analog are summarized.

IT **135219-43-1D**, Poststatin, derivs.
RL: BIOL (Biological study)
(for treatment of systemic lupus erythematosus and Alzheimer's disease, as prolyl endopeptidase inhibitors)

IT **72162-84-6**, Prolyl endopeptidase
RL: BIOL (Biological study)
(inhibitors of, poststatins as, for treatment of systemic lupus erythematosus and Alzheimer's disease)

L13 ANSWER 12 OF 17 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:612981 HCAPLUS
DOCUMENT NUMBER: 117:212981
TITLE: Preparation of peptides containing .beta.-amino-.alpha.-ketoacid groups as **protease** inhibitors
INVENTOR(S): Yamada, Fumika; Sugimura, Hideo; Someno, Tetsuya; Muraoka, Yasuhiko; Tsuda, Makoto; Takeuchi, Tomio; Aoyanagi, Takaaki
PATENT ASSIGNEE(S): Nippon Kayaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 04149166 | A2 | 19920522 | JP 1990-272183 | 19901012 <-- |

OTHER SOURCE(S): MARPAT 117:212981

AB XNHCHRCOCOY [I; X = H, amino, (un)protected peptide or amino acid residue; Y = (un)protected peptide or amino acid residue; R = (un)substituted Ph or naphthyl] are prepd. as **protease** inhibitors (no data). Thus, N-acylation of threo-3-amino-2-hydroxy-4-(o-methoxyphenyl)butyric acid with di-tert-Bu dicarbonate in 1N NaOH and dioxane and condensation of the

resultant threo-3-tert-butoxycarbonylamino-2-hydroxy-4-(o-methoxyphenyl)butyric acid (64.5% yield) with H-D-Val-Val-OCH2Ph.CF3CO2H in the presence of 1-hydroxybenzotriazole and DCC in CH2Cl2 gave 80.5% N-[(3RS)-3-tert-butoxycarbonylamino-2-hydroxy-4-(o-methoxyphenyl)butanoyl]-D-leucyl-L-valine benzyl ester which was oxidized with pyridine trifluoroacetate, DCC, and DMSO in benzene to give 73.1% N-[(3RS)-3-tert-butoxycarbonylamino-2-oxo-4-(o-methoxyphenyl)butanoyl]-D-leucyl-L-valine benzyl ester. A total of 18 I were prepd.

IT **9001-92-7, Protease**
RL: USES (Uses)
(inhibitors, arylaminooxobutyric acid-contg. peptides)

IT **144138-91-0P 144138-92-1P 144138-93-2P**
**144138-94-3P 144138-95-4P 144138-96-5P**
**144138-97-6P 144138-98-7P 144138-99-8P**
**144139-00-4P 144139-01-5P 144139-02-6P**
**144139-03-7P 144139-04-8P 144139-05-9P**
**144139-06-0P 144139-07-1P 144139-17-3P**
**144179-34-0P 144179-35-1P 144179-36-2P**
**144179-37-3P 144179-38-4P 144179-39-5P**
**144179-40-8P 144179-44-2P 144179-45-3P**
**144179-46-4P 144179-47-5P 144179-48-6P**
**144179-49-7P 144179-50-0P 144179-51-1P**
**144179-52-2P 144179-53-3P 144239-26-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as **protease** inhibitor)

L13 ANSWER 13 OF 17 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:236175 HCAPLUS
DOCUMENT NUMBER: 116:236175
TITLE: Preparation of peptides containing 3-amino-2-oxoalkanoic acid residue as endopeptidase inhibitiors
INVENTOR(S): Takeuchi, Tomio; Aoyanagi, Takaaki; Muraoka, Yasuhiko; Tsuda, Makoto; Nagai, Machiko
PATENT ASSIGNEE(S): Microbiochemical Research Foundation, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 16 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 04001140 | A2 | 19920106 | JP 1990-99174 | 19900413 <-- |

OTHER SOURCE(S): MARPAT 116:236175
AB Peptides contg. NHCHR1COCO (R1 = satd. or unsatd. hydrocarbyl) fragments are prepd. Et3N and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide perchlorate were added to a soln. of Boc-D-Leu-OH. H2O, L-valine benzyl ester tosylate, and N-hydroxybenzotriazole in CH2Cl2 under cooling and the mixt. was stirred at room temp. to give 97.8% Boc-D-Leu-Val-OCH2Ph, which as the CF3CO2H salt was coupled with (2R,3S)-3-p-methoxybenzyloxycarbonyl)amino-2-hydroxypentanoic acid and further coupled with valine twice, and subsequent oxidn., to give Z-Val-Val-(S)-NHCHEtCOCO-D-Leu-Val-OCH2Ph, which showed IC50 of 1 .mu.g/mL against prolyl endopeptidase, 75 .mu.g/mL against elastase, and 100 .mu.g/mL against cathepsin B.

IT **9001-92-7**, Endopeptidase
RL: USES (Uses)
(inhibitors, aminooxoalkanoyl peptides)

IT **135219-43-1P 135219-45-3P 135219-46-4P**
**135219-47-5P 135219-48-6P 135219-49-7P**
**135219-50-0P 135219-52-2P 135219-53-3P**

**135219-54-4P 135219-55-5P 135219-56-6P**
**135219-57-7P 135219-58-8P 135219-59-9P**
**135219-60-2P 135219-61-3P 135219-62-4P**
**135270-54-1P 135355-22-5P 141187-10-2P**
**141187-11-3P 141187-12-4P 141187-13-5P**
**141187-14-6P 141187-15-7P 141270-17-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as endopeptidase inhibitor)

L13 ANSWER 14 OF 17 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:675338 HCAPLUS
DOCUMENT NUMBER: 115:275338
TITLE: Poststatin, a new inhibitor of prolyl endopeptidase, produced by Streptomyces viridochromogenes MH534-30F3. I. Taxonomy, production, isolation, physico-chemical properties and biological activities
AUTHOR(S): Aoyagi, Takaaki; Nagai, Machiko; Ogawa, Keiji; Kojima, Fukiko; Okada, Mayumi; Ikeda, Takako; Hamada, Masa; Takeuchi, Tomio
CORPORATE SOURCE: Inst. Microb. Chem., Tokyo, 141, Japan
SOURCE: Journal of Antibiotics (**1991**), 44(9), 949-55
CODEN: JANTAJ; ISSN: 0021-8820
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Poststatin, a new inhibitor of prolyl endopeptidase (PEP) was discovered in the fermn. broth of S. viridochromogenes MH534-30F3. It was purified by Dianion HP-20, Sephadex LH-20 and YMC-gel (ODS-A) column chromatog. and then isolated as a colorless powder. Poststatin has the mol. formula C26H47N5O7. The IC50 value of poststatin against the PEP of partially purified porcine kidney was 0.03 .mu.g/mL. It has low acute toxicity. No deaths occurred after i.v. injection of 250 mg/kg of this agent to mice.
IT **72162-84-6**, Prolyl endopeptidase
RL: PROC (Process)
(inhibition of, by poststatin from Streptomyces viridochromogenes)
IT **135219-43-1**, Poststatin
RL: BIOL (Biological study)
(prolyl endopeptidase inhibitor, from Streptomyces viridochromogenes)

L13 ANSWER 15 OF 17 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:673762 HCAPLUS
DOCUMENT NUMBER: 115:273762
TITLE: Poststatin, a new inhibitor of prolyl endopeptidase, produced by Streptomyces viridochromogenes MH534-30F3. II. Structure determination and inhibitory activities
AUTHOR(S): Nagai, Machiko; Ogawa, Keiji; Muraoka, Yasuhiko; Naganawa, Hiroshi; Aoyagi, Takaaki; Takeuchi, Tomio
CORPORATE SOURCE: Inst. Microb. Chem., Tokyo, 141, Japan
SOURCE: Journal of Antibiotics (**1991**), 44(9), 956-61
CODEN: JANTAJ; ISSN: 0021-8820
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Poststatin, a new inhibitor of prolyl endopeptidase, has been isolated from the culture broth of S. viridochromogenes MH534-30F3. The structure of poststatin was defined as L-valyl-L-valyl-3-amino-2-oxovaleryl-D-leucyl-L-valine by anal. of spectral properties and chem. studies of poststatin and its derivs. The .alpha.-keto group of postine in poststatin plays the most important role on the inhibitory mechanism.
IT **74506-45-9**, Prolyl endopeptidase
RL: PROC (Process)
(poststatin of Streptomyces viridochromogenes inhibition of)
IT **135219-43-1**, Poststatin
RL: BIOL (Biological study)
(structure of and prolyl endopeptidase inhibition by, of Streptomyces

viridochromogenes)

L13 ANSWER 16 OF 17 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:515068 HCAPLUS
DOCUMENT NUMBER: 115:115068
TITLE: Synthesis and endopeptidase inhibitory activity of poststatin and its analogs
AUTHOR(S): Tsuda, Makoto; Muraoka, Yasuhiko; Nagai, Machiko; Aoyagi, Takaaki; Takeuchi, Tomio
CORPORATE SOURCE: Inst. Microb. Chem., Tokyo, 141, Japan
SOURCE: Peptide Chemistry (**1991**), 28th, 223-8
CODEN: PECHDP; ISSN: 0388-3698
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A symposium report on the prepn. and endopeptidase inhibitory activity of poststatin [H-Val-Val-Pos-D-Leu-Val-OH; Pos = (S)-H2NCHEtCOCO2H] and its analogs.
IT **72162-84-6**, Prolyl endopeptidase
RL: USES (Uses)
(inhibitors, poststatin and its analogs)
IT **135219-43-1DP**, analogs **135219-43-1P**, Poststatin
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and endopeptidase-inhibiting activity of)

L13 ANSWER 17 OF 17 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:490647 HCAPLUS
DOCUMENT NUMBER: 115:90647
TITLE: Microbial preparation of postostatin and chemical synthesis of related compounds
INVENTOR(S): Takeuchi, Tomio; Aoyagi, Takaaki; Hamada, Masa; Naganawa, Hiroshi; Muraoka, Yasuhiko; Ogawa, Keiji; Nagai, Machiko; Tsuda, Makoto
PATENT ASSIGNEE(S): Zaidan Hojin Biseibutsu Kagaku Kenkyu Kai, Japan
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9012805 | A1 | 19901101 | WO 1990-JP491 | 19900413 <-- |
| W: JP, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE | | | | |
| EP 423358 | A1 | 19910424 | EP 1990-905686 | 19900413 <-- |
| R: DE, FR, GB, IT | | | | |
| EP 672648 | A1 | 19950920 | EP 1995-106762 | 19900413 <-- |
| EP 672648 | B1 | 19980923 | | |
| R: DE, FR, GB, IT | | | | |
| US 5162500 | A | 19921110 | US 1990-613759 | 19901207 <-- |
| PRIORITY APPLN. INFO.: | | | JP 1989-94328 | 19890415 |
| | | | EP 1990-905686 | 19900413 |
| | | | WO 1990-JP491 | 19900413 |

OTHER SOURCE(S): MARPAT 115:90647
AB Postostatin (I) and its analogs X-NHCR1HCOCOY ((protected peptide residues, (NH2-protected) amino acid residues; R1 = (un)satd. hydrocarbons; configuration of R1-bonded C atom is S or RS; Y = (protected peptide residues,s (HO2C-protected) amino acid residues), potent endopeptidase inhibitors having pharmaceutical applications, are manufd. by Streptomyces or by chem. synthesis. S. viridochromogenes was cultured by conventional methods at 27.degree. for 4 days. From 12.5-L culture filtrate, I 20 mg was recovered after a series of chromatog. and HPLC. I

(m.p. 169-171.degree.) having a defined peptide structure was also characterized with IR and NMR. Chem. synthesis of I and a variety of analogs, e.g. Z-L-phenylalanyl-(RS)-3-amino-2-oxopentanoyl-D-leucyl-L-valine tert Bu ester from amino acids and evaluation of their activities against elastase, cathepsin B, prolyl endopeptidase were also described. A pharmaceutical tablet compn. contg. I was given.

IT **9001-92-7**, Endopeptidase **9004-06-2**, Elastase
**74506-45-9**, Prolyl endopeptidase
RL: BIOL (Biological study)
(inhibitors of, postostatin and analogs as)

IT **135219-43-1P**, Postostatin
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(manuf. of, with Streptomyces, as endopeptidase inhibitor)

IT **135219-44-2P 135219-45-3P 135219-46-4P**
**135219-47-5P 135219-48-6P 135219-49-7P**
**135219-50-0P 135219-51-1P 135219-52-2P**
**135219-53-3P 135219-54-4P 135219-55-5P**
**135219-56-6P 135219-57-7P 135219-58-8P**
**135219-59-9P 135219-60-2P 135219-61-3P**
**135219-62-4P 135270-54-1P 135355-22-5P**
RL: PREP (Preparation)
(postostatin analog, prepn. of, as endopeptidase inhibitor)

IT **135219-43-1DP**, analogs
RL: PREP (Preparation)
(prepn. of, as endopeptidase inhibitors)

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E39 THROUGH E143 ASSIGNED

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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 15 NOV 2002 HIGHEST RN 473758-49-5
DICTIONARY FILE UPDATES: 15 NOV 2002 HIGHEST RN 473758-49-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

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Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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DR   9001-21-2, 139074-64-9, 75603-19-9, 83682-98-8


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L14  ANSWER 1 OF 98  REGISTRY  COPYRIGHT 2002 ACS
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     asparaginyl-3-amino-2-oxobutanoyl-, phenylmethyl ester (9CI)  (CA INDEX
     NAME)
FS   PROTEIN SEQUENCE; STEREOSEARCH
MF   C35 H54 N6 O10
SR   CA
LC   STN Files:   CA, CAPLUS, USPATFULL

Absolute stereochemistry.
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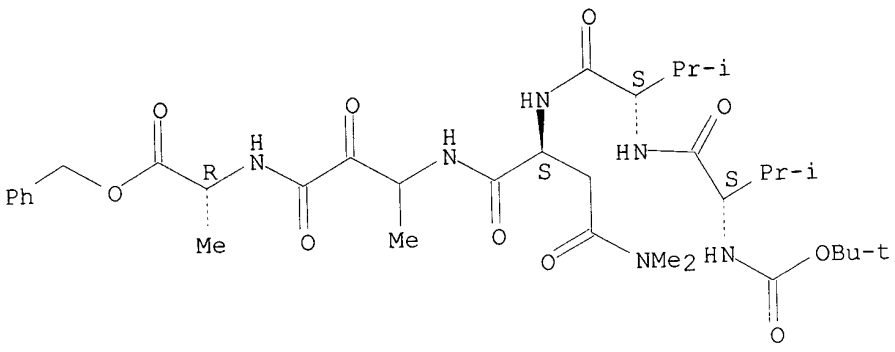


1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

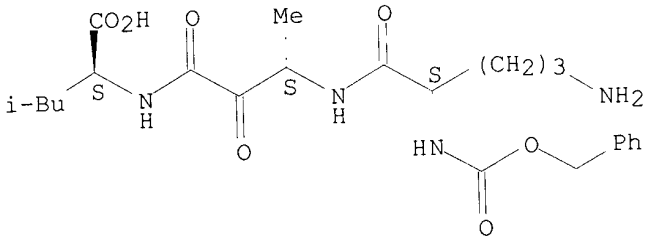
REFERENCE 1: 129:122872

L14 ANSWER 2 OF 98 REGISTRY COPYRIGHT 2002 ACS
RN **199467-27-1** REGISTRY
CN 2-Oxa-4,7,11-triazatridecan-13-oic acid, 5-(3-aminopropyl)-8-methyl-12-(2-methylpropyl)-3,6,9,10-tetraoxo-1-phenyl-, [5S-(5R*,8R*,12R*)]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H34 N4 O7 . C2 H F3 O2
SR CA
LC STN Files: CA, CAPLUS

CM 1

CRN 199467-26-0
CMF C23 H34 N4 O7

Absolute stereochemistry.



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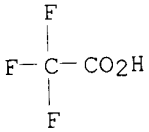


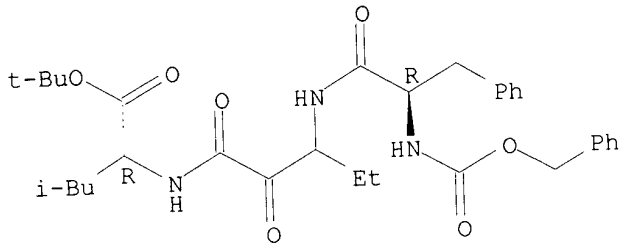
1 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 128:35014

L14 ANSWER 7 OF 98 REGISTRY COPYRIGHT 2002 ACS
RN **182966-22-9** REGISTRY
CN D-Leucine, N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-2-oxo-3-aminopentanoyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H43 N3 O7
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



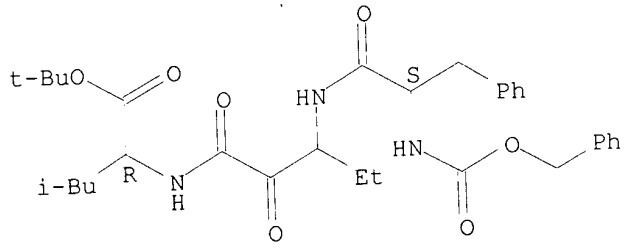

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 125:301554

L14 ANSWER 12 OF 98 REGISTRY COPYRIGHT 2002 ACS
RN **182742-42-3** REGISTRY
CN D-Leucine, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-2-oxo-3-aminopentanoyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H43 N3 O7
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

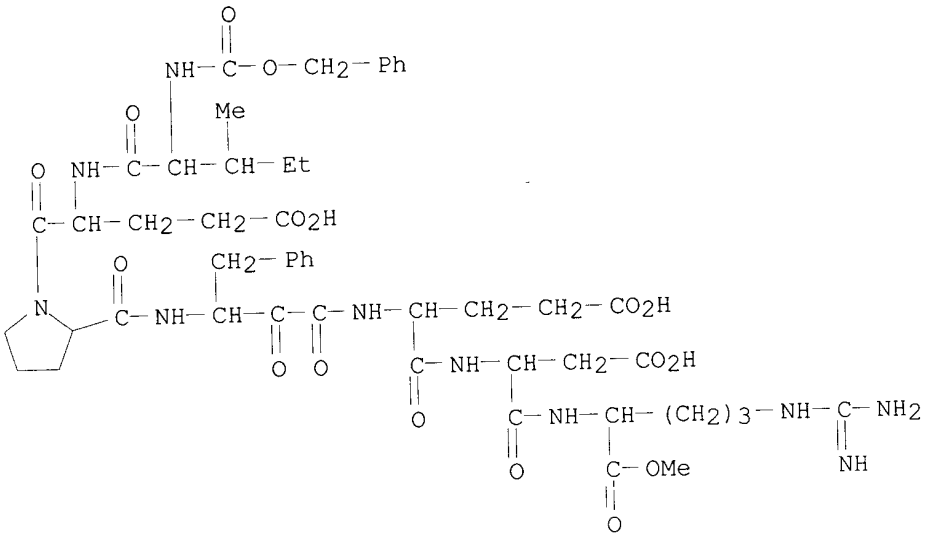



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 125:301554

L14 ANSWER 19 OF 98 REGISTRY COPYRIGHT 2002 ACS
RN **166267-80-7** REGISTRY
CN L-Arginine, N-[(phenylmethoxy)carbonyl]-L-isoleucyl-L-.alpha.-glutamyl-L-prolyl-2-oxo-4-phenyl-3-aminobutanoyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl-, 7-methyl ester (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF C50 H68 N10 O17
SR CA
LC STN Files: CA, CAPLUS



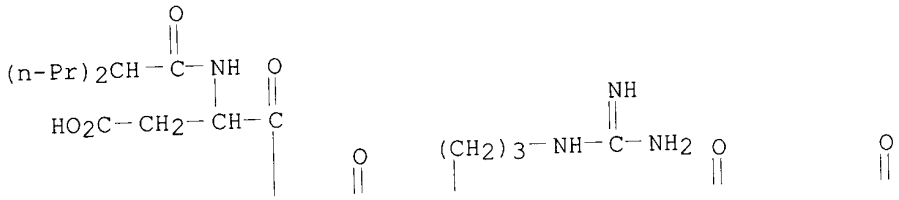
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 123:106201

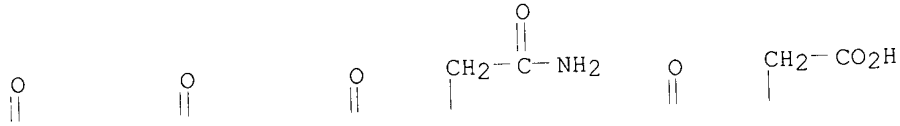
L14 ANSWER 20 OF 98 REGISTRY COPYRIGHT 2002 ACS
RN **166247-65-0** REGISTRY
CN L-Leucine, N-(1-oxo-2-propylpentyl)-L-.alpha.-aspartyl-L-prolyl-N6-(aminoiminomethyl)-2-oxo-(S)-3,6-diaminohexanoylglycylglycylglycylglycylglycylglycyl-L-asparaginylglycyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-isoleucyl-L-prolyl-L-.alpha.-glutamyl-L-tyrosyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN CVS 995
FS PROTEIN SEQUENCE
DR 174970-72-0, 175278-85-0
MF C94 H137 N23 O34
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, CA, CAPLUS, DRUGNL, DRUGUPDATES, PHAR, USPATFULL

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

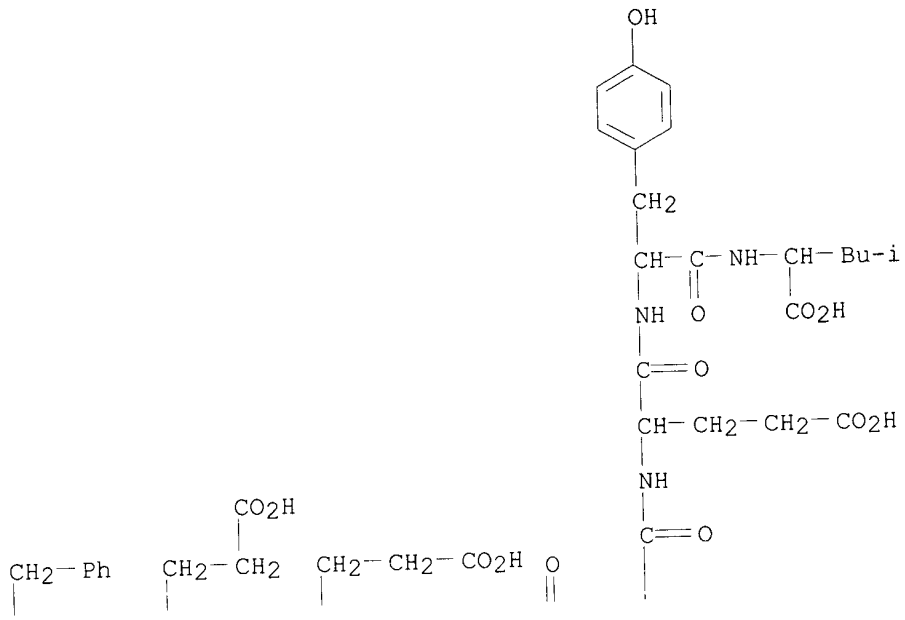
PAGE 1-A



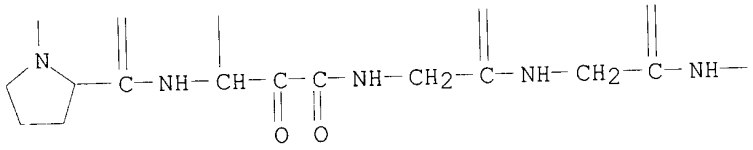
PAGE 1-B



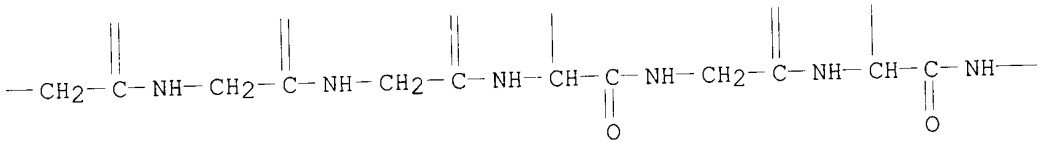
PAGE 1-C



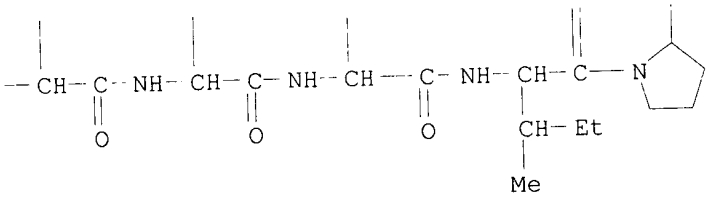
PAGE 2-A



PAGE 2-B



PAGE 2-C



4 REFERENCES IN FILE CA (1962 TO DATE)
4 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 127:293640

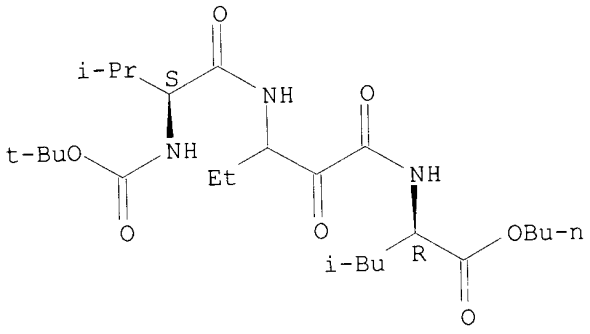
REFERENCE 2: 124:282995

REFERENCE 3: 124:250214

REFERENCE 4: 123:144645

L14 ANSWER 21 OF 98 REGISTRY COPYRIGHT 2002 ACS
RN **160772-55-4** REGISTRY
CN D-Leucine, N-[(1,1-dimethylethoxy)carbonyl]-L-valyl-2-oxo-3-aminopentanoyl-, butyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN D-Leucine, N-[(1,1-dimethylethoxy)carbonyl]-L-valyl-2-oxo-DL-3-aminopentanoyl-, butyl ester
FS STEREOSEARCH
MF C25 H45 N3 O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



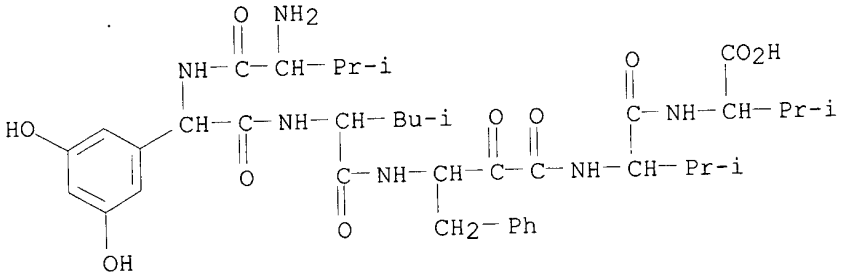

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 122:131140

L14 ANSWER 23 OF 98 REGISTRY COPYRIGHT 2002 ACS
RN **157381-55-0** REGISTRY
CN L-Valine, L-valyl-2-(3,5-dihydroxyphenyl)glycyl-L-leucyl-2-oxo-4-phenyl-3-aminobutanoyl-L-valyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF C39 H56 N6 O10
SR CA
LC STN Files: CA, CANCERLIT, CAPLUS, MEDLINE

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

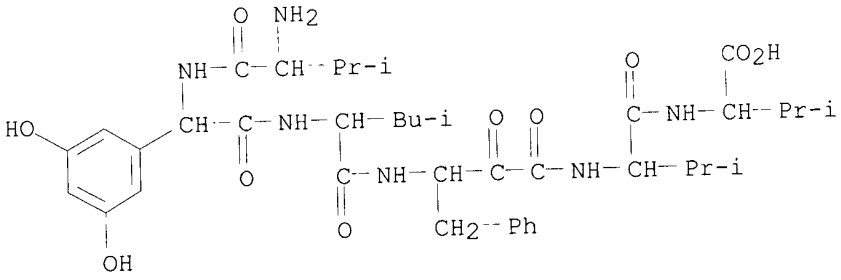


1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 121:250735

L14 ANSWER 25 OF 98 REGISTRY COPYRIGHT 2002 ACS
RN **157341-55-4** REGISTRY
CN L-Valine, L-valyl-2-(3,5-dihydroxyphenyl)glycyl-L-leucyl-2-oxo-4-phenyl-3-aminobutanoyl-L-valyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF C39 H56 N6 O10
SR CA
LC STN Files: CA, CAPLUS

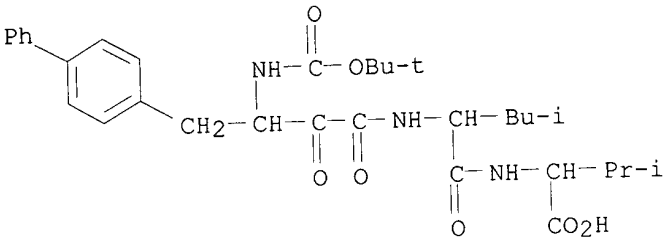
**RELATED SEQUENCES AVAILABLE WITH SEQLINK**



1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 121:250735

L14 ANSWER 27 OF 98 REGISTRY COPYRIGHT 2002 ACS
RN **144239-26-9** REGISTRY
CN L-Valine, N-[N-[4-[1,1'-biphenyl]-4-yl-3-[[(1,1-dimethylethoxy)carbonyl]amino]-1,2-dioxobutyl]-D-leucyl]-, (R)- (9CI) (CA INDEX NAME)
MF C32 H43 N3 O7
SR CA
LC STN Files: CA, CAPLUS



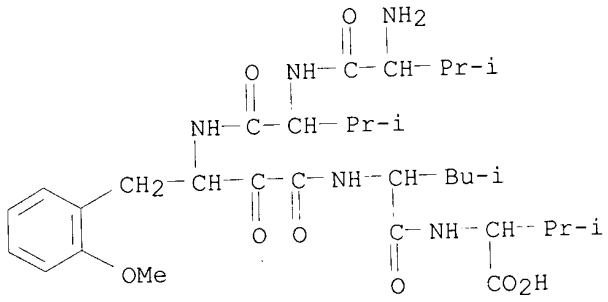
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 117:212981

L14 ANSWER 28 OF 98 REGISTRY COPYRIGHT 2002 ACS
RN **144179-53-3** REGISTRY
CN L-Valine, L-valyl-L-valyl-4-(2-methoxyphenyl)-2-oxo-(S)-3-aminobutanoyl-D-leucyl-, monohydrochloride (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF C32 H51 N5 O8 . Cl H
SR CA
LC STN Files: CA, CAPLUS

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

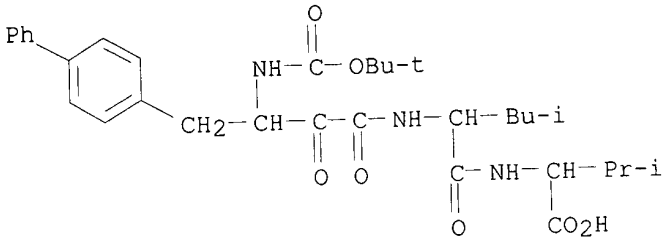


● HCl

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 117:212981

L14 ANSWER 45 OF 98 REGISTRY COPYRIGHT 2002 ACS
RN **144139-17-3** REGISTRY
CN L-Valine, N-[N-[4-[1,1'-biphenyl]-4-yl-3-[[(1,1-dimethylethoxy)carbonyl]amino]-1,2-dioxobutyl]-D-leucyl]-, (S)- (9CI) (CA INDEX NAME)
MF C32 H43 N3 O7
SR CA
LC STN Files: CA, CAPLUS



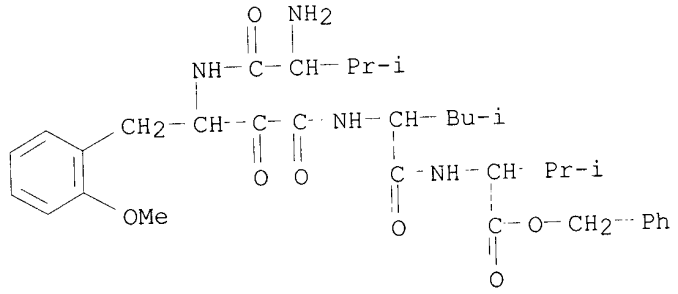
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 117:212981

L14 ANSWER 54 OF 98 REGISTRY COPYRIGHT 2002 ACS
RN **144138-99-8** REGISTRY
CN L-Valine, L-valyl-4-(2-methoxyphenyl)-2-oxo-(R)-3-aminobutanoyl-D-leucyl-, phenylmethyl ester, monohydrochloride (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF C34 H48 N4 O7 . Cl H
SR CA
LC STN Files: CA, CAPLUS

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**



● HCl

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 117:212981

L14 ANSWER 63 OF 98 REGISTRY COPYRIGHT 2002 ACS
RN **144114-21-6** REGISTRY
CN Retropepsin (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Avian leukosis virus proteinase
CN E.C. 3.4.23.16
CN Endogenous retroviral proteinase
CN FIV proteinase
CN Gag Protease

CN HIV aspartyl protease
CN HIV protease
CN HIV proteinase
CN HIV-1 aspartyl protease
CN HIV-1 aspartyl proteinase
CN HIV-1 protease
CN HIV-1 proteinase
CN HIV-1 virus aspartyl proteinase
CN HIV-1 virus protease
CN HIV-2 protease
CN HTLV proteinase
CN HTLV-1 proteinase
CN Human immunodeficiency virus protease
CN Mason-Pfizer monkey virus protease
CN Moloney murine leukemia virus protease
CN Retroproteinase
CN Rous sarcoma virus protease
CN RSV proteinase
CN Simian immunodeficiency virus aspartyl proteinase
MF Unspecified
CI COM, MAN
SR CA
LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, CA, CAPLUS, CASREACT, CIN, PROMT, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
2570 REFERENCES IN FILE CA (1962 TO DATE)
90 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2574 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:310904

REFERENCE 2: 137:310820

REFERENCE 3: 137:306865

REFERENCE 4: 137:306498

REFERENCE 5: 137:304747

REFERENCE 6: 137:304740

REFERENCE 7: 137:304331

REFERENCE 8: 137:304328

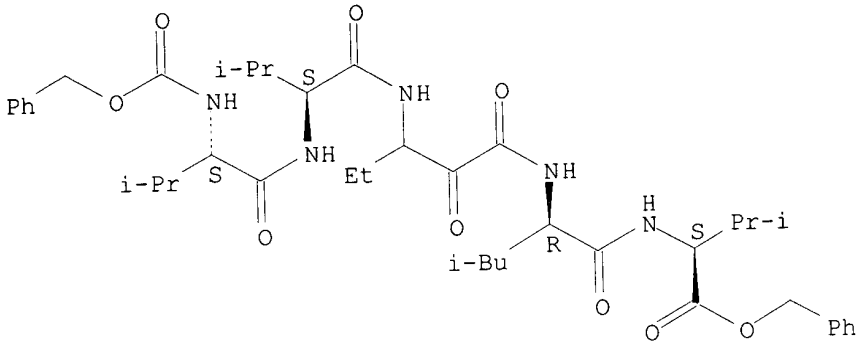
REFERENCE 9: 137:304327

REFERENCE 10: 137:304178

L14 ANSWER 64 OF 98 REGISTRY COPYRIGHT 2002 ACS
RN **141270-17-9** REGISTRY
CN L-Valine, N-[(phenylmethoxy)carbonyl]-L-valyl-L-valyl-2-oxo-3-aminopentanoyl-D-leucyl-, phenylmethyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Valine, N-[(phenylmethoxy)carbonyl]-L-valyl-L-valyl-2-oxo-DL-3-aminopentanoyl-D-leucyl-, phenylmethyl ester
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C41 H59 N5 O9
SR CA
LC STN Files: CA, CAPLUS

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

Absolute stereochemistry.



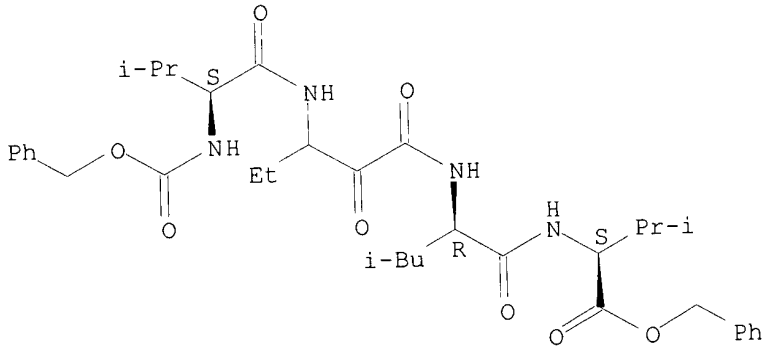
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 116:236175

L14 ANSWER 65 OF 98 REGISTRY COPYRIGHT 2002 ACS
RN **141187-15-7** REGISTRY
CN L-Valine, N-[(phenylmethoxy)carbonyl]-L-valyl-2-oxo-3-aminopentanoyl-D-leucyl-, phenylmethyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Valine, N-[(phenylmethoxy)carbonyl]-L-valyl-2-oxo-DL-3-aminopentanoyl-D-leucyl-, phenylmethyl ester
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C36 H50 N4 O8
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 122:131140

REFERENCE 2: 116:236175

L14 ANSWER 71 OF 98 REGISTRY COPYRIGHT 2002 ACS
RN **139691-88-6** REGISTRY

CN Proteinase, assembly protein precursor-processing (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Assemblin
CN Assembly protein precursor-processing proteinase
CN Cytomegalovirus protease
CN Gene UL26 protease
CN Herpes simplex virus 1 proteinase Pra
CN Herpesvirus serine proteinase
CN HSV 1 protease
CN Human cytomegalovirus maturational proteinase
CN Human cytomegalovirus protease
CN Human cytomegalovirus proteinase
CN Kaposi's sarcoma-associated herpesvirus protease
CN Varicella-zoster virus gene 33 proteinase
MF Unspecified
CI MAN
SR CA
LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, CA, CAPLUS, IPA, PROMT, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
122 REFERENCES IN FILE CA (1962 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
122 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:307189

REFERENCE 2: 137:290752

REFERENCE 3: 137:288515

REFERENCE 4: 137:194828

REFERENCE 5: 137:163117

REFERENCE 6: 137:75611

REFERENCE 7: 136:366247

REFERENCE 8: 136:243681

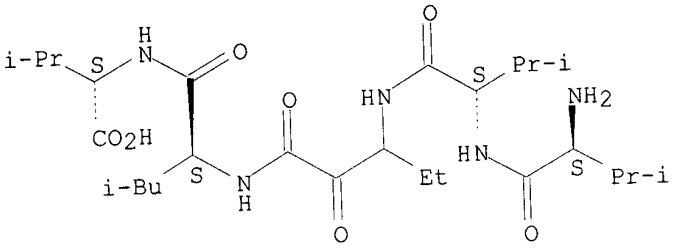
REFERENCE 9: 136:184121

REFERENCE 10: 136:184115

L14 ANSWER 72 OF 98 REGISTRY COPYRIGHT 2002 ACS
RN **135355-22-5** REGISTRY
CN L-Valine, L-valyl-L-valyl-2-oxo-3-aminopentanoyl-L-leucyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C26 H47 N5 O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

Absolute stereochemistry.



4 REFERENCES IN FILE CA (1962 TO DATE)
4 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 125:301554

REFERENCE 2: 122:131140

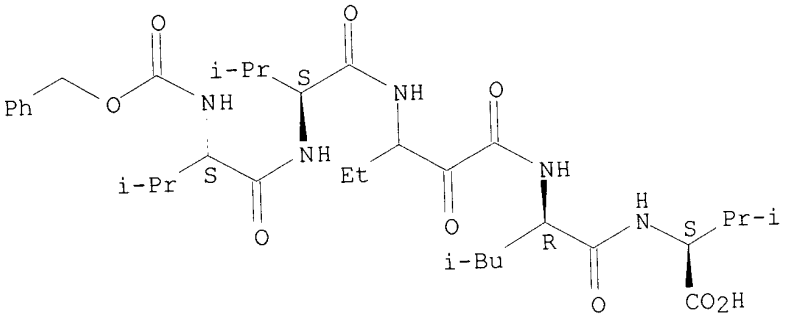
REFERENCE 3: 116:236175

REFERENCE 4: 115:90647

L14 ANSWER 73 OF 98 REGISTRY COPYRIGHT 2002 ACS
RN **135270-54-1** REGISTRY
CN L-Valine, N-[(phenylmethoxy)carbonyl]-L-valyl-L-valyl-2-oxo-3-aminopentanoyl-D-leucyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C34 H53 N5 O9
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

Absolute stereochemistry.



4 REFERENCES IN FILE CA (1962 TO DATE)
4 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 125:301554

REFERENCE 2: 122:131140

REFERENCE 3: 116:236175

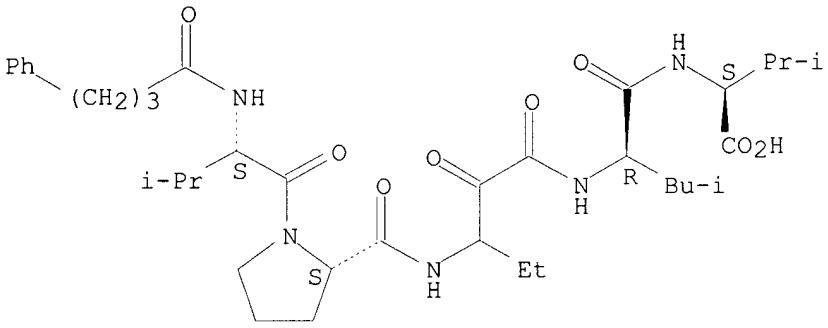
REFERENCE 4: 115:90647

L14 ANSWER 74 OF 98 REGISTRY COPYRIGHT 2002 ACS
RN **135219-62-4** REGISTRY

CN L-Valine, N-(1-oxo-4-phenylbutyl)-L-valyl-L-prolyl-2-oxo-3-aminopentanoyl-D-leucyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C36 H55 N5 O8
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

Absolute stereochemistry.



4 REFERENCES IN FILE CA (1962 TO DATE)
4 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 125:301554

REFERENCE 2: 122:131140

REFERENCE 3: 116:236175

REFERENCE 4: 115:90647

L14 ANSWER 94 OF 98 REGISTRY COPYRIGHT 2002 ACS
RN **129737-17-3** REGISTRY
CN Proteinase inhibitor, TAP (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Tick anticoagulant peptide
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISINSIGHT, AGRICOLA, BIOSIS, CA, CAPLUS, CIN, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
40 REFERENCES IN FILE CA (1962 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
40 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:88551

REFERENCE 2: 134:290412

REFERENCE 3: 134:130256

REFERENCE 4: 134:14520

REFERENCE 5: 132:318927

REFERENCE 6: 132:290352

REFERENCE 7: 132:231982

REFERENCE 8: 132:216407

REFERENCE 9: 132:133895

REFERENCE 10: 131:55770

L14 ANSWER 95 OF 98 REGISTRY COPYRIGHT 2002 ACS
RN **97501-92-3** REGISTRY
CN Chymase (9CI) (CA INDEX NAME)
OTHER NAMES:
CN E.C. 3.4.21.39
CN Lymphocyte chymase I
CN Mast cell protease I
CN Mast cell protease-1
CN Mast cell proteinase I
CN Mast cell serine proteinase I
CN Proteinase RMCP-1
CN Proteinase, mast cell serine, chymase
CN Proteinase, mast cell serine, I
CN Rat mast cell protease 1
DR 82599-73-3
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CIN, EMBASE, PROMT, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
593 REFERENCES IN FILE CA (1962 TO DATE)
9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
596 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:310922

REFERENCE 2: 137:306642

REFERENCE 3: 137:292657

REFERENCE 4: 137:276301

REFERENCE 5: 137:273345

REFERENCE 6: 137:261783

REFERENCE 7: 137:261469

REFERENCE 8: 137:260705

REFERENCE 9: 137:246022

REFERENCE 10: 137:230420

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RN **72162-84-6** REGISTRY
CN Peptidase, proline endo- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN APP protein endopeptidase
CN Chorionic peptidase-1
CN E.C. 3.4.21.26
CN Endoprolylpeptidase

CN Oligopeptidase B
CN Postproline endopeptidase
CN Postproline-cleaving enzyme
CN Proline endopeptidase
CN Proline-specific endopeptidase
CN Prolyl endopeptidase
CN Prolyl oligopeptidase
CN Tc80 prolyl endopeptidase
CN Tc80 protease
DR **74506-45-9**
MF Unspecified
CI MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CIN, EMBASE, PROMT, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
581 REFERENCES IN FILE CA (1962 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
585 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:309902

REFERENCE 2: 137:307036

REFERENCE 3: 137:304644

REFERENCE 4: 137:291657

REFERENCE 5: 137:279043

REFERENCE 6: 137:274061

REFERENCE 7: 137:241671

REFERENCE 8: 137:228604

REFERENCE 9: 137:182334

REFERENCE 10: 137:165380

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RN **37205-61-1** REGISTRY
CN Proteinase inhibitor (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Antiproteinase
CN Fu Gu Tai
CN Protease inhibitor
DR 139074-30-9, 144716-05-2, 144132-75-2
MF Unspecified
CI MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CEN, CIN, DIOGENES, EMBASE, IFICDB, IFIPAT, IFIUDB, PROMT, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
4741 REFERENCES IN FILE CA (1962 TO DATE)
90 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4752 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:309479

REFERENCE 2: 137:306026

REFERENCE 3: 137:306025

REFERENCE 4: 137:293697

REFERENCE 5: 137:293080

REFERENCE 6: 137:291850

REFERENCE 7: 137:277305

REFERENCE 8: 137:275965

REFERENCE 9: 137:273829

REFERENCE 10: 137:262109

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RN **9004-06-2** REGISTRY
CN Elastase (9CI) (CA INDEX NAME)
OTHER NAMES:
CN E.C. 3.4.21.11
CN E.C. 3.4.21.36
CN E.C. 3.4.21.37
CN E.C. 3.4.24.65
CN E.C. 3.4.4.7
CN Elastase 2
CN Elaszym
CN Macrophage metalloelastase
CN Matrix metalloprotease 12
CN Matrix metalloproteinase-12
CN Medullasin
CN MMP 12
CN Neutrophil Elastase
CN Pancreatopeptidase E
CN Peptidase, pancreato-, E
CN Proteinase, bone marrow serine
DR 9001-21-2, 139074-64-9, 75603-19-9, 83682-98-8
MF Unspecified
CI COM, MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MRCK*, NAPRALERT, NIOSHTIC, PHAR, PIRA, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
7362 REFERENCES IN FILE CA (1962 TO DATE)
257 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
7367 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:316147

REFERENCE 2: 137:315996

REFERENCE 3: 137:311201

REFERENCE 4: 137:309438

REFERENCE 5: 137:308602

REFERENCE 6: 137:307868

REFERENCE 7: 137:307141

REFERENCE 8: 137:306026

REFERENCE 9: 137:305963

REFERENCE 10: 137:293477